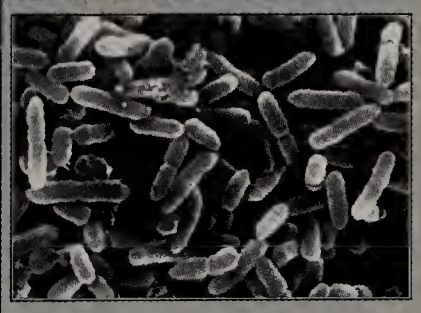
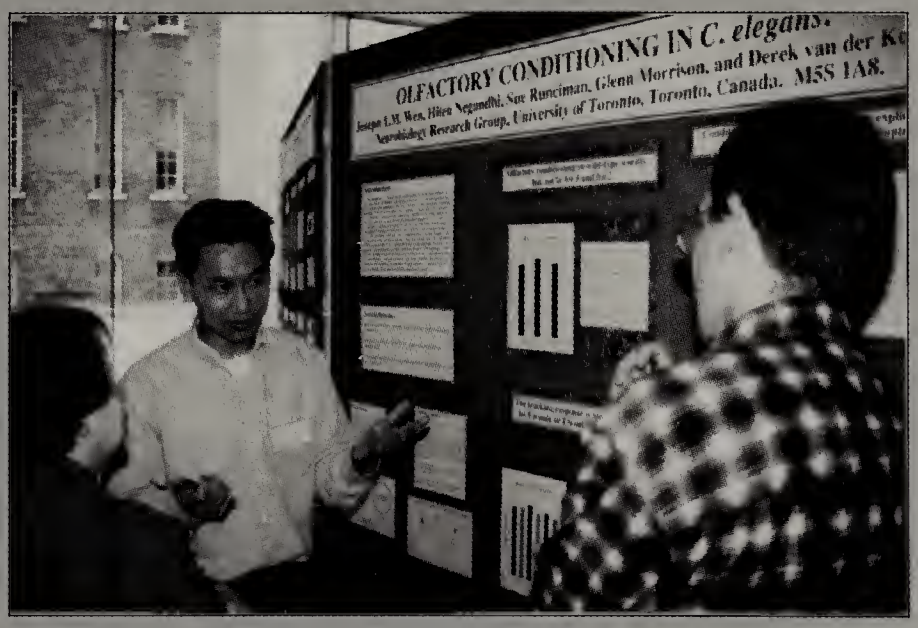
January 1997 Volume 74, Supplement

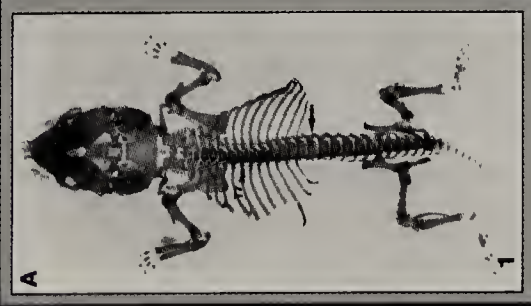
Medical Journal

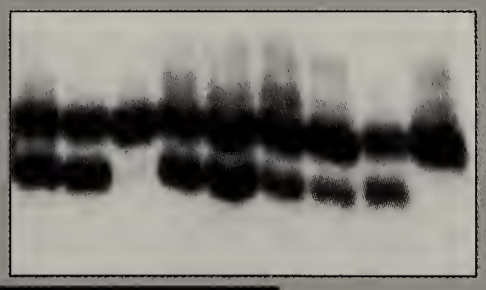
Undergraduate Medical Research

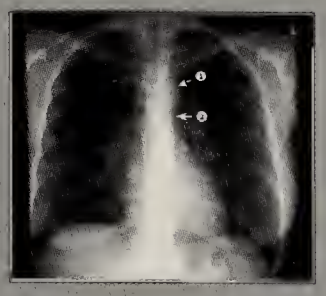
at the University of Toronto




OLFACTORY CONDITIONING IN C. elegans.
Joseph I.M. Wen, Hiten Nagandhi, Sue Runciman, Glenn Morrison, and Derek van der K
Neurobiology Research Group, University of Toronto, Toronto, Canada. M5S 1A8.







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University of Toronto

Medical Student Research Day

January 14, 1997

1:00-2:00 pm — **Keynote Speaker: Dr. Gary Levy**
"New Insights into the Genetic Basis of Fulminant Liver Failure"
Medical Sciences Building, Room 3154

2:00-4:30 pm — Student Poster Presentations and Competition
Medical Sciences Building, Stone Lobby

4:45-5:30 pm — Presentations by winners of 1996 Research Day Competition
Medical Sciences Building, Room 3154

Michael Heiber
Winner of the George Brown Memorial Award - Experienced Researcher (Basic) Category, and the Sigma XI Award for Overall Excellence in Research, Poster Presentation at the 37th Annual National Student Research Forum (NSRF), Galveston, Texas, 1996.
"Cloning and characterization of a human gene encoding a novel G protein-coupled receptor"

Ally-Khan Somani
Winner of the George Brown Memorial Award - MD/PhD Student Researcher (Basic or Clinical) Category, and 2nd Place for Outstanding Presentation in Biochemistry at the 22th Annual Eastern Student Research Forum (ESRF), Miami, Florida, 1996.
"The PTP1C tyrosine phosphatase regulates the tyrosine kinase activity of the src proto-oncogene"

Eric Chu
Winner from the Department of Medicine
"The effects of the stress response in a rat model of sepsis"

MEDICAL STUDENT DAY RAFFLE DRAW

5:30 pm — ***Award Presentation and Wine and Cheese Reception***

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Keynote Speaker: *DR. GARY A. LEVY, MD, FRCP(C)*

Dr. Levy graduated from medical school at the University of Toronto in 1973. He completed his training in hepatology at the University of Toronto in 1978 and undertook post-doctoral training in Immunology at the Scripps Clinic and Research Foundation from 1978-1981. Dr. Levy founded and became the Medical Director of the Liver Transplant Unit in 1987 at the Toronto Hospital and University of Toronto and in 1991 he organized and co-founded the Multi Organ Transplant Unit at the Toronto Hospital and the University of Toronto.

He is currently a Full Professor in the Departments of Medicine and Surgery and the Director of Gastroenterology at the University of Toronto and Director of the Multi Organ Transplant Unit at the Toronto Hospital and University of Toronto.

He has organized and now heads a research group of 11 principle investigators which is focused on studying cellular and molecular mechanisms of inflammation. His research, funded by the Medical Research Council of Canada and the National Institutes of Health has focused on immune-mediated mechanisms of organ injury due to viruses, alloantigens, and xenoantigens. He has published over 200 original articles, and 20 books and book chapters.

He has received a number of honours including election to the American Society for Clinical Investigation, the Goldie Prize in Medicine, the Canadian Association of Gastroenterology Visiting Research Professorship, and the University of Toronto, Department of Medicine Research Award for outstanding contributions to research. He is a member of the following editorial boards: Transplantation Science, Liver Transplantation and Surgery and Current Opinion in Organ Transplantation.

MESSAGE FROM THE DEAN

Welcome to the 11th Annual Medical Student Research Day. This is an important day for the Faculty of Medicine, because it provides an opportunity for our undergraduate medical students to showcase the wide spectrum of research projects they have completed, often during summer fellowships. These projects range from investigations of basic cellular activity to studies of clinical applications in hospitals and community involvement, revealing the many career pathways open to today's medical students.

Taking a research project from concept to completion provides undergraduates with a stimulating learning experience, giving them the opportunity to discover if they have the self-discipline, dedication and creative thinking required to be a successful investigator. As Dean, I am proud to say that many of our undergraduate medical students do have these qualities. Take a look at their research projects and you will see what I mean. 1996 is the 75th anniversary of the discovery of insulin by Banting, Best, Collip and Macleod and we continue to be inspired by the impact that research has on the practice of medicine. It is my hope that many of the students involved in today's Medical Student Research Day will continue that tradition. Congratulations to all the participants - and many thanks to the faculty members who made this year's event possible.

Arnie Aberman

MESSAGE FROM THE VICE-DEAN, EDUCATION

The Faculty of Medicine Undergraduate Medical Student Research day provides an opportunity for students to display the results of their research. Each summer approximately 100 medical students receive scholarships through the Faculty of Medicine enabling them to work on projects in basic science laboratories and clinical investigative settings. Their research follows diverse paths from basic molecular biology to clinical outcomes and community health. Approximately 40% of the students who apply are funded and present their work on Research Day. Selection is based on scholarship and merit of the proposed research. Students in the MD-Ph.D. research program also present their work at Medical Student Research Day. The top-rated students in the categories of basic and clinical research, receive an all-expense paid trip to the Annual Medical Student Research Forum (USA) in Galveston, Texas, in April, representing our Faculty. In addition the Department of Medicine supports the top-rated student (in either the clinical or basic science category), supervised by one of its members, to attend the same meeting.

Why do students wish to extend their professional training into the realm of biomedical research? There are many reasons including scientific curiosity and extension of previous engagement in research. More than 30% of students now entering Medicine at Toronto hold graduate degrees. Nonetheless for many of the students, whose abstracts are contained in this journal, their first taste of research came after they entered the medical program. All the research presented at Research Day has been carried out while students are enrolled in the undergraduate medical program or the MD/Ph.D. program. Many of these students have and will contribute to scientific papers published in peer-reviewed journals. Some will seek future career development as clinician-scientists, by entering graduate or post-graduate research programs during or after clinical specialty training. The Faculty of Medicine at the University of Toronto is a major focus of basic and clinical investigation in Canada. The 11th annual Medical Student Research Day shows how effectively our medical students take advantage of this rich learning environment.

Students participating in research day have taken time out of a demanding professional training program to prepare and present their posters. Health care professionals engaged in research are challenged to maintain a balance between clinical and investigative responsibilities. The students who participate in Research Day begin to experience this sometimes difficult, yet highly rewarding, duality. The posters displayed at the Research Day demonstrate the fruits of their self-discipline, dedication and creativity.

The students and Faculty are indebted to the Medical Student Committee who worked so hard and efficiently in the planning and preparation for Research Day.

Members of the Research Day Committee
Names: *April Boyd, Charles Dela Cruz, David Hwang, David Klein, Catherine Mason, Wei Mei Pang, Christine Pun, Tom Ransom, Frank Ritacca, Ally-Khan Somani.*

Andrew D. Baines
for the Research Day Coordinating Committee

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B1

Elucidation of a region of the Na/glucose cotransporter involved in the coupling of Na binding to glucose transport. Bryan Lo*, Melvin Silverman. MRC Group in Membrane Biology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada, M5S 1A8.

Thc Na/glucose cotransporter uses the Na electrochemical gradient to drive the transport of sugar across intestinal .and renal brush border membranes. By combining the techniqucs of site-directed mutagenesis and chemical modification of specific amino acid side chains, we havc elucidated structure/function relationships that underlie the coupling of Na to glucose transport. Bcginning with the cloned rabbit transporter (rSGLT1), each amino acid in the loop connecting putative transmembrane helices IV and V was replaced individually with cysteine (Cys). The mutant proteins werc expressed in *Xenopus Laevis* oocytes and using the two electrode voltagc clamp method, the effect of thc Cys substitution on the function of the transporter was assayed. All of the Cys mutants demonstrated sugar induced sodium currents and were therefore processed properly to the plasma membrane of the oocytes. Some of the Cys mutants, however, demonstrated alterations in both their steady-statc and pre-stcady state kinetics that suggested a role for this region in the proper functioning of the transporter. Moreover, some of the Cys mutants became sensitive to inhibition by certain watcr soluble methanethiosulphonate derivatives, compounds which specifically target and modify the sulphydryl group of cysteines. Since the wild type rSGLT1 was previously determined to be insensitive towards such compounds, it was concluded that the introduced cystcine was being reacted and the resulting modification was the reason for the inhibition. Detailed analysis of the nature of the inhibition has provided convincing evidence that this region of the protcin is directly involved in the coupling of Na binding to glucose transport.

CV1

Incidence of neurologic events in patients with carotid artery disease and coronary artery bypass grafts -influence of severity of carotid stenosis and concurrent carotid endarterectomy. K. Ahmad*, L.L. Mickleborough, M. Tamariz. Division of Cardiovascular Surgery, The Toronto Hospital, 200 Elizabeth St. M5G 2C4

Carotid artery disease is a frequently encountered pre-operative complication in patients undergoing coronary artery bypass grafting (CABG). Appropriate management of carotid disease in CABG is the subject of some controversy with respect to the correct operative intervention and subsequent risk of cerebral ischemic events in such patients. Approaches include: isolated CABG, combined carotid endarterectomy (CEA) and CABG, and staged CABG-CEA. The purpose of this study is to evaluate the effect of severity of carotid disease, and combined CABG-CEA vs. isolated CABG on the frequency of follow-up neurologic events in patients who underwent pre-operative carotid screening. **Methods:** Data were prospectively collected on 170 patients who underwent preoperative carotid screening for suspected external carotid artery disease. 116 patients without significant carotid disease (<70% stenosis) underwent isolated CABG (group I). 33 patients had asymptomatic, unilateral, significant (>70%) stenosis (group II) and also underwent isolated CABG. 21 patients underwent combined CABG-CEA on the basis of >70% carotid stenosis with neurologic symptoms or severe bilateral disease. (Group III) All procedures were performed by a single surgeon. Telephone follow up of patients and caregivers was conducted to document post operative survival, morbidity and neurologic events. **Results:** 170 patients were followed up with a mean follow up time of 73.5 months. 5 year survival in groups I, II, and III were, respectively, 87%, 97%, and 77%. Total mortality in groups I, II, and III were: 27%, 18%, and 28%. Incidence of follow up neurological events was 14% in group I, 21% in group II, and 0% in group III. Overall, 9 patients in group I (8%), 3 patients in group II (9%), and 0 patients in group III (0%) were found to have strokes in follow up. Patients did not differ significantly on the basis of: age >60 years, left ventricular ejection fraction <20%, perioperative myocardial infarction, and ascending aortic disease. **Conclusion:** These results appear to support the use of combined CABG-CEA in selected patients to reduce the risk of neurologic events in follow up. Larger trials of the combined procedure are warranted to fully evaluate the procedure's efficacy and further refine patient selection.

CV2

SUTURE-INDUCED STRESSES MAY PROMOTE INTIMAL HYPERPLASIA AT GRAFT-ARTERY ANASTOMOSES.
P.D. Ballyk[1,2*], C. Walsh[3], J. Butany[1,4] and M. Ojha[1,2], Faculty of Medicine[1], Institute of Biomedical Engineering[2], Institute of Aerospace Studies[3] and The Toronto Hospital[4], University of Toronto, Toronto, Canada, M5S 1A4

Many vascular bypass grafts become obstructed several years post-operatively due to distal anastomotic intimal hyperplasia (DAIH). It has been suggested that unusual hemodynamics and/or graft-artery compliance mismatch may promote DAIH, however, these factors are not uniformly distributed at the anastomosis, and thus cannot explain the near uniform distribution of DAIH around the suture-line. A potentially important factor which has been neglected in all previous analyses of this phenomenon is the effect of the sutures on the intramural stress distribution. Arterial healing after surgery is quite slow (~ 6 mo.), and most of the early strength of the anastomosis is provided by the sutures. Our hypothesis is that the stress concentrations created by the sutures may be an important inciting factor for DAIH.

Human saphenous vein aortocoronary bypass grafts (CABG) were obtained at autopsy. Patent CABG specimens were fixed in 10% formalin and serially sectioned to demonstrate the suture-line and changes around it. The tissue was then embedded in paraffin and 5 micron sections were cut and stained with H&E and elastic trichrome stains. The intramural stress distribution at the vein-artery anastomosis was calculated before and after suture-line healing using our large strain finite element model of vascular mechanics (Ballyk et al. 1996).

The histological sections demonstrate that most of the early (< 8 wks) rapid intimal thickening is centered around the sutures, where our numerical simulations calculate large stress concentrations. After the anastomosis has healed (> 8 mo.), the high rate of suture-line proliferation is no longer in evidence histologically, and the numerical calculations indicate a dramatic reduction in the anastomotic stress concentrations. These results indicate that the early rapid hyperplasia seen in the first few post-surgical months may be promoted by suture-induced stress injury.

CV3

Outcome of Coronary Stenting in the Real World

Brian Blew*, Leonard Schwartz. Division of Cardiology, The Toronto Hospital, Toronto, Canada.

The average 7 month event and angiographic restenosis rates for the stent arm of Benestent I and STRESS I were 20% and 27% respectively with a mortality rate of 1.2%. However, the patients and lesions in these studies were highly selected & may not reflect the general experience. We studied 100 consecutive patients (pts) who underwent coronary stent deployment for the first time. ***Population & Stent data:*** age 62±11.3yrs; 77 male, 23 female; prior Coronary Artery Bypass Graft (CABG) 23pts; prior Percutaneous Translumenal Coronary Angioplasty (PTCA) 42 pts; 125 stents, (89Palmaz-Schatz & 36 Gianturco-Roubin). ***Indications for stenting by lesion:*** suboptimal balloon result 41%; bailout 21%; restenotic lesion 20%; bypass graft 9%; other 9%. ***Clinical success rate*** was 93% with 1 death, 1 CABG, 4 non Q-wave MI's & 1 subacute thrombosis. ***Follow-up*** was obtained clinically in all patients & by quantitative coronary angiography (QCA) in 88 patients (93% of those eligible) at 25±11 wks. There were 20 pts with late coronary events: 5 cardiac deaths; 6 CABG's; 7 PTCA's; 2 MI's yielding 27 pts with early or late events including an overall cardiac mortality rate of 6%.

QCA	Baseline	Post Stent	1°Gain	Follow-up
ref (mm)	3.37±0.69	3.34±0.60		3.26±1.06
MLD (mm)	1.11±0.54	2.96±0.56	1.86±0.65	1.79±0.99
% DS	67.8±13.3	14.1±8.9	53.8±17.2	47.3±24

ref =reference vessel; MLD = minimum lumen diameter; DS = diameter stenosis

Inspite of a 1° gain comparable to that of Benestent/STRESS, the angiographic restenosis rate was appreciably higher @ 43%. Only 16 pts fulfilled the criteria of these trials and their clinical & angiographic restenosis rates were 25%. ***In conclusion,*** pts receiving intracoronary stents in practice have a worse clinical outcome and a higher angiographic restenosis rate that pts in trials. This is likely due to less favourable clinical & lesion characteristics.

CV4

ECHOCARDIOGRAPHIC EVALUATION OF LEFT ATRIAL SIZE AND FUNCTION POST-MYECTOMY IN PATIENTS WITH OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY.

C. Chiam*, B. O'Kelly. Division of Cardiology, Faculty of Medicine, University of Toronto.

Obstructive hypertrophic cardiomyopathy is caused by basal septal hypertrophy and systolic anterior motion of the mitral valve. Surgical removal of a portion of the basal septum (myectomy) abolishes the resultant left ventricular outflow tract (LVOT) gradient and may reduce left atrial (LA) size. However, the effect of myectomy on left atrial function is unknown. Accordingly we retrospectively measured the effect of myectomy on **LA size** [by 2D-echocardiography: LA diameter (LAD-cm), LA volume (LAV-cm^3)], and **LA function** [by 2D echo: LA fractional shortening (LAFS-%), LA emptying volume (LAEV-%) and by Doppler echo: mitral inflow A-wave height (MVA-cm/s)]. Nine patients were studied (age 50±14 years, 6 male) pre- and 31±2 3 months post-myectomy.

Results: Myectomy reduced the LVOT gradiant (pre 66±31 mm Hg, post 11±17 mm Hg, $p< 0.01$) and mitral regurgitation jet area (pre 4±3 cm^2 , post 2±2 cm^2, p=0.18).

	LAD	LAV	LAFS	LAEV	MVA
Pre	42.3	63.7	15.5	43.3	79.8
Post	37.1*	38.4*	16.0	42.5	76.7

(*:P<0.05, Wilcoxin Rank Sum Test)

Thus, post-myectomy LA size is reduced and LA function is unchanged.

Conclusion: Myectomy reduces LA size but fails to improve LA function in patients with obstructive hypertrophic cardiomyopathy. This failure may contribute to persistent exercise intolerance in post-myectomy patients.

CV5

DIFFERENT MECHANISMS MAY UNDERLIE ELAFIN AND ALPHA$_1$ PROTEINASE INHIBITOR REPRESSION OF IL-1ß STIMULATED FIBRONECTIN SYNTHESIS IN PORCINE CORONARY ARTERY SMOOTH MUSCLE CELLS.

B. Cowan* and M. Rabinovitch. Division of Cardiovascular Research, The Hospital for Sick Children, Faculty of Medicine, University of Toronto, Canada M5G 1X8

Increased expression of fibronectin (FN), interleukin-1ß (IL-1ß), and serine elastase activity, in coronary arteries (CA) of donor hearts, are features of heterotopic cardiac transplantation (HCT) and functionally associated with CA neointimal formation. *In vitro* experiments in donor CA smooth muscle cells (SMC) demonstrated that endogenous IL-1ß is responsible for the induction of FN and other work suggests that κ-elastin peptides promotes an IL-1ß-mediated increase in FN synthesis. In these studies, we compared the ability of the elastase inhibitors elafin and α_1-proteinase inhibitor (α_1-PI), to suppress IL-1ß-mediated SMC FN synthesis and determined whether the mechanism was related to repression of elastin peptides. We optimized IL-1ß-induction of FN and demonstrated a dose dependent inhibition with both inhibitors. This was associated with an IL-1ß-induction of SMC elastin peptides by western immunoblot and a marked reduction in peptide production in response to α_1-PI. Human leukocyte elastase-generated porcine aortic elastin derived peptides (EDP) bypassed elafin inhibitory effects at 10 ng/ml (undetectable by immunoblotting) and synergized with IL-1ß in the stimulation of FN, but could not overcome the effects of α_1-PI. Elafin and α_1-PI similarly reduced the aurocrine production of IL-1ß, again suggesting an additional inhibitory effect of α_1-PI which could not be overcome by EDP. While it is possible that the inhibitory effect of α_1-PI may be mediated by an induction of IL-1 receptor antagonist (IL-1ra), its effects could not be reversed by an IL-1ra neutralizing antibody, nor could we detect immunoreactive IL-1ra in treated cultures. We cannot, however, exclude lack of cross-reactivity of the human anti-IL-1ra antibody to the porcine species. Taken together, these data suggest that nanogram quantities of low molecular weight enzymatically-generated EDPs stimulate CA SMC FN synthesis and synergize with IL-1ß. While elafin may block the effects of IL-1ß induced EDP, α_1-PI may act by a different mechanism.

CV6

The Effects of Allogeneic Fibroblast Transplantation into Scarred Rat Myocardium

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Previously we have shown that transplanted cardiomyocytes formed cardiac tissue in a myocardial scar, limited scar expansion and improved heart function as compared with non-transplanted controls. The aim of the present study was to determine whether transplanted fibroblasts could survive and improve function in the scarred heart. Scar tissue in the left ventricular free wall was generated in the adult rat heart by cryoinjury. Four weeks after cryoinjury cultured fetal rat fibroblasts or culture medium was injected into the scar tissue of transplanted (n=9) and control rats (n=9), respectively. Heart function was measured in both groups eight weeks after cryoinjury using a Langendorff preparation. Histology was performed to determine the size of the scar and presence of angiogenesis. At eight weeks after cryoinjury, the scar size comprised a significant portion of the left ventricular free wall surface area in both groups. Grossly, fibroblast transplantation reduced the aneurysm formation and wall thinning observed in controls. Diffuse angiogenesis and survival of myocardial cells was observed in transplanted though not culture medium injected controls. Systolic pressure was greater ($p<0.05$) in transplanted (117 ± 3 mmHg) than control (108 ± 4 mmHg) group. In conclusion, allogeneic transplanted fibroblasts: 1) limited scar expansion, 2) resulted in angiogenesis within the scar site, 3) increased survival of native myocardial cells and 4) enhanced peak systolic pressure.

CV7

NITRIC OXIDE MEDIATES POST-TRANSCRIPTIONAL REGULATION OF FIBRONECTIN SYNTHESIS IN DUCTUS ARTERIOSUS SMOOTH MUSCLE CELLS C.Mason* and M.Rabinovitch. Hospital for Sick Children, University of Toronto, Ontario, Canada M5G 1X8.

Neointimal formation, a feature of vascular disease, occurs as a normal developmental process in the fetal ductus arteriosus (DA). We have shown that migration of SMC is dependent on increased fibronectin (FN) synthesis, regulated at the post-transcriptional level by interaction of LC-3 protein with the FN mRNA 3'-untranslated region (UTR). Nitric oxide (NO) is an important signalling molecule produced in the DA. We investigated whether differences in NO production in DA compared to aorta (Ao) SMC cause enhanced DA FN synthesis. Using FACS analysis following dihydrorhodamine loading we demonstrated greater reactive oxygen species production in DA compared to Ao SMC, largely related to an 8-fold increase ($p<0.01$) in NO production, as assessed by nitrite accumulation. Inhibition of ROS production by DPI or NO by L-NMMA both resulted in a 40% decrease in FN synthesis ($p<0.01$) in DA SMC to the level found in Ao SMC, but did not affect FN synthesis in Ao SMC. In both DA and Ao SMC cultures, however, addition of the NO donor, SNAP, increased FN synthesis by 45% ($p<0.01$). Northern analysis demonstrated no change in steady state FN mRNA in DA SMC following L-NMMA or SNAP, suggesting that NO mediates upregulation of FN at the post-transcriptional level. Furthermore, levels of LC-3 were increased with SNAP and decreased with L-NMMA on western blots. Our data indicate that increased NO production in DA SMC directs cell phenotype through post-transcriptional regulation of FN, and potentially other genes associated with SMC motility and neointimal formation.

CV8

STRESS-INDUCED ST ELEVATION IN Q-WAVE LEADS INDICATES INTERMEDIATE PROBABILITY OF ISCHEMIA DESPITE ABSENCE OF THE USUAL CORRELATES OF ISCHEMIC ST DEPRESSION. G.Y.Oudit*, R.J. Burns. Division of Cardiology, The Toronto Hospital, Faculty of Medicine, University of Toronto, Canada M5G 1X8.

Stress-induced ST elevation(STE) in nonQ-wave leads indicates transmural ischemia, but in Q-wave leads is often considered to reflect LV aneurysm with stress LV dilation. We compared 71 consecutive STE cases in 7075 ^{201}Tl SPECT patients (pts, 1%) to matched (for age, sex, stress protocol, presence & location of Q-waves) 'ischemic' ST depression (STD) pts from the same cohort. ^{201}Tl was interpreted by visual consensus and quantitatively. STE pts had larger stress defects than STD pts (43.5±16.2 %LV vs 33.5±19.4 %LV, p=0.001) but similar extent, degree, and distribution of ^{201}Tl reversibility (TR). Overall 46/71 STE pts vs 61/71 STD pts had TR (p=0.003). In Q-wave pts 37/61(61%) STE vs 48/58(83%) STD had TR (p=0.007). STE was associated with TR by: longer interval post revascularization (in 30 pts, 60±66 vs 10±12 mo., p=0.004), maximal STE in a nonQ-wave lead (p=0.03), and absence of Q-waves (p<0.05), but not by: stress-induced ΔΣQRS amplitude, mets, stress-induced chest pain, or stress heart rate and BP Δ's. We also compared 'TR' vs 'no TR' cases in STE and STD groups:

	STE:TR	STE:no TR	p	STD:TR	STD:no TR	p
mets	8.4±1.7	7.3±2.2	NS	7.5±1.8	8.9±1.2	.005
# leads	2.7±1.9	2.4±1.5	NS	4.9±1.7	3.8±1.0	.014
ΣΔST	+10±7	+10±6	NS	-8±4	-6±2	.024
ΣΔST/HR	+.09±.04	+.08±.04	NS	-.06±.04	-.04±.01	.001
ΔΣQRS/mets	1.1±3.6	0.5±3.0	NS	1.2±0.9	0.7±0.2	.001
LV dilation	19/46(.35)	7/25(.28)	NS	15/61(.25)	0/10(0)	.023

leads = no. leads with ST change; ΣΔST = sum of ST changes(mm); ΣΔST/HR = ΣΔST ÷ maximum heart rate; ΔΣQRS/mets = increase in summed QRS amplitude (mm) ÷ mets; LV dilation = transient on ^{201}Tl stress images. CONCLUSION: Stress-induced STE in Q-leads implies intermediate(.61) probability of ischemia which is not predicted by nonscintigraphic data. This therefore constitutes an appropriate indication for myocardial perfusion imaging. STE and TR are not associated with known correlates of stress-induced ischemia. This suggests different mechanisms of STE ischemia (*e.g.* high segmental wall stress, focal/peri-infarct ischemia) and/or of TR (*e.g.* defect stress-expansion and contraction rather than reversibility *per se*).

CV9

Tricuspid Valve Surgery in Patients with Congenital Heart Defects

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Traditionally, tricuspid valve repair and replacement surgery has been associated with relatively high perioperative morbidity and mortality, with poor long term results. The purpose of this study was to review the outcome and incidence of atrial arrhythmias in patients (pts) with complex congenital heart defects who underwent tricuspid valve surgery between 1971 and 1995 at the Hospital for Sick Children and the Toronto Hospital. Data was obtained for 87 pts (39 males [45%]; 48 females [55%]) through retrospective chart review of all available hospital records. The majority of these pts had either Ebstein's anomaly (19), Tetralogy of Fallot (13), Congenitally Corrected Transposition (16), ASD (11), or VSD (9). Median age at time of surgery was 30 (1 to 71) years. Forty-eight (55%) pts underwent tricuspid valve repair, 18 (21%) underwent bioprosthetic valve replacement, and 21 (24%) underwent mechanical valve replacement. Seventy-eight (90%) pts were in NYHA Class II-IV within one year prior to operation.

Results: 44 (51%) pts had symptomatic sustained atrial arrhythmia's within one year prior to tricuspid valve surgery. Of these, 32 (73%) had atrial fibrillation or atrial flutter, 5 (11%) had SVT, and 7 (16%) had Wolff-Parkinson-White (WPW) syndrome. Following tricuspid surgery, 26 pts (59%) had recurrence of atrial arrhythmias. Furthermore, 7 pts who were in sinus rhythm preoperatively developed atrial arrhythmias late after surgery. Perioperative mortality was 3.5% (1 intraoperative death, 2 early hospital deaths), while the late mortality rate was 7% (6 pts). Survival following surgery was 92 ± 3% at 5 years, and 85 ± 5% at 10 years.

Conclusions: Surgical intervention does not restore sinus rhythm in the majority of pts with preoperative arrhythmias. Tricuspid valve surgery can be carried out with acceptably low risk of perioperative mortality, and leads to good long term outcome in pts with complex congenital heart malformations.

CH1

WOMEN AND DEPRESSION. Rose Bilotta. Faculty of Medicine, University of Toronto, Canada M5G 1X8. (Supervisor: Dr. Donna Stewart, Women's Health Program, The Toronto Hospital)

The purpose of this study was to research depression in women 20-64 years of age living in Metropolitan Toronto. Methods included reviewing the literature, examining existing statistics [Ontario Health Survey of 1990 (OHS), Mental Health Supplement of 1991, and 1991 Census] and collecting qualitative data via two community surveys [key providers at community agencies and users of the Mood Disorder Association]. A demographic profile of Metro Toronto women was created with 1991 Census data. MAPINFO was used to map the participating agencies and clients by forward sortation area (FSA).

Two questionnaires were designed -- one for key providers and one for clients. Both surveys asked for the respondent's opinion on what they felt *causes* women to become depressed, what *helps* them overcome it, and what *protects* women against the onset of depression. In addition, the client-questionnaire asked to comment on what caused them to become depressed and what advice they would give other women about depression.

The study results can be summarized into three main findings. 1) Sixteen percent of women (20-64 years of age) in Metro Toronto reported a "low" Well-Being Index (OHS 1990). Since the Well-Being Index correlates with clinical depression, this implies that about 120,636 women in Metro Toronto may be vulnerable or suffer from depression. 2) The survey opinions on what causes, helps and protects depressed women are validated by the literature. 3) People with higher levels of education tend to use self-help groups and read more about the management of their depression.

The recommendations based on this study are summarized in the acronym "REFORM" (Table 1)

Table 1: RECOMMENDATIONS

Restructure current services to improve access.
Educate/Empower women to seek appropriate help
Foster multiculturally sensitive services
Outline services in a user friendly catalogue
Relocate services in appropriate demographic areas
MDs identify DEPRESSION, treat or refer as needed.

CH2

COST-IDENTIFICATION ANALYSIS OF PRONOUNCEMENT OF DEATH IN THE FIELD. M. Cheung*, L. J. Morrison. Division of Emergency Medicine, Sunnybrook Health Sciences Centre, Faculty of Medicine, University of Toronto.

Over the past 20 years, basic life support (BLS) and paramedic (ALS) programmes have been developed to respond to potentially reversible cases of cardiac arrest. However, despite many refinements to our emergency medical services, overall national survival rates from out-of-hospital cardiac arrests are less than 5%. The low chance of survival of certain cardiac arrests and the ability of paramedics to identify predictors of unsuccessful resuscitations have opened the debate on the 'futility' of transporting these cases to the emergency department (ED) for further resuscitative efforts.

Paramedics (ALS) in the Toronto setting are allowed to pronounce death in the field when the patient is obviously deceased or as directed by a Base Hospital Physician. In the same situation, however, the BLS provider is obliged by law to resuscitate and transport all patients to the closest hospital.

Although some studies have examined the effectiveness of pre-hospital care in terms of saved lives and outcomes, little research has been done to estimate the costs of these programmes. This study analyzed whether pronouncement of death in the field by paramedics is a cost effective alternative to BLS assessment and transport to the ED. Twenty cases of field pronouncements were matched to cases of death pronouncement in the ED. The costs of ALS and BLS care were obtained from Metro Ambulance on a dollars-per-unit-basis, while emergency physician billing and emergency nurse work measurement assessments were obtained in each case of in-hospital pronouncment. The direct costs involved in the provision of care were calculated and compared, using the chi-square test to determine statistical significance between the matched pairs.

Presently, ALS providers are only dispatched to cardiac arrests if they are within a defined area adjacent to the distress call. The results of this analysis may lead to changes in dispatch criteria and may increase ALS access to all cardiac arrest patients or may emphasize the need to provide base hospital physician input for all levels of providers.

CH3

HEALTH CARE DELIVERY IN DHARAMSALA, INDIA: CONTRIBUTIONS FROM TRADITIONAL TIBETAN AND WESTERN MEDICINE. Cecil D. Hahn*
International Health Program, Faculty of Medicine, University of Toronto, Canada M5S 1A8

The goal of this study was to investigate how traditional Tibetan and western medicine contribute to health care delivery in Dharamsala, a Tibetan settlement of 20,000 inhabitants in the northern Indian province of Himachal Pradesh.

Objectives: 1) to study the attitudes of physicians and patients towards traditional Tibetan and western medicine, including the perceived strengths and weaknesses of both medical systems; 2) to investigate how physicians from Tibetan and western medical traditions contribute to the delivery of health care in this community.

Methods: Structured interviews were conducted with patients and physicians at outpatient clinics of the traditional Tibetan Medical Institute and the western Delek Hospital. Subjects were asked to characterize the particular strengths and weaknesses of both medical traditions and describe their patterns of utilization. In addition, interviews were conducted with the directors of both medical centres and with the Minister of Health of the Tibetan government in exile, to review their policies for the coordinated delivery of traditional Tibetan and western medical care.

Results: Patients and physicians in this community generally agreed that western medicine is most beneficial for the treatment of acute illnesses and for quick symptomatic relief. They felt that traditional Tibetan medicine, although slower-acting, cures illnesses 'from the root' and may provide a more beneficial long-term outcome with fewer side-effects than does western medicine. Physicians at the traditional Tibetan and western medical centres were found to cooperate extensively in the exchange of medical expertise and in the collaborative treatment of patients. However, there were few established guidelines at the two centres for a coordinated approach to the major public health concerns of the community.

CH4

WHAT PREVENTS PATIENTS FROM OBTAINING PREVENTIVE HEALTH SERVICES: A STUDY OF NON-RESPONDERS TO A HEPATITIS-B VACCINE MAILING. L. Mah*, S. Shafir, M. Evans, J. Bloom. Department of Family and Community Medicine, The Toronto Hospital, Faculty of Medicine, University of Toronto, Canada M6J 3S3

Background: Identifying patients' reasons for non-response to mailings is essential for improving their effectiveness. In a letter campaign for hepatitis-B immunization, cost was hypothesized to have been a major factor for non-response in a population unaccustomed to paying for medical services. **Methods**: 4922 letters encouraging hepatitis-B vaccination were mailed between March and June 1996 to 15 to 35 year old patients of a family practice unit. A telephone survey of non-responders was conducted to evaluate the dissemination of the mailing and to identify patient-perceived barriers to hepatitis-B immunization. **Results**: 195 telephone interviews were completed. 63.1% remembered both the mailing and the content of the mailing. The two most common self-reported reasons for not obtaining the hepatitis-B vaccine were "not being at risk" (26.1%) and previous hepatitis-B vaccination (22.6%). Cost was mentioned in only 3.5% of cases as a self-reported reason for not being immunized. **Conclusions**: The mailing was successful in disseminating information about the hepatitis-B vaccine. Risk perception was a major barrier for immunization, and not the cost of the vaccine as hypothesized. To encourage behavioral change in patients, future campaigns should focus on the design of mailings and ensure that messages are directive and clear.

CH5

SUPPORTIVE CARE SERVICES AND LUNG CANCER PATIENTS: USAGE AND BARRIERS
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As part of a larger study examining quality of life in lung cancer patients, a sample of 101 patients (49 women, 52 men) was surveyed about their use of, and perceived barriers to, 33 different supportive care services. For each service, subjects were asked to indicate one of the following: it was used and useful; it was used and not useful; it would be useful. The categories of services found to be the most used and useful were: talk with or get help from a professional (52%); talk with or get help from family and/or friends (45%); and acquire information (34%). The categories of services most likely to be used were: upkeep of self or surroundings (36%); talk with or get help from a professional (30%); and acquire information (30%). The most frequently cited barriers to services were: didn't know where to get help (15%); didn't like to ask for help (15%); and didn't know how to get help (10%). Relationships between use of services and quality of life, coping, depression, age and medical characteristics indicated: use of services is more likely with decreased quality of life; younger subjects are more likely to use professional and bureaucratic services; individuals who employ task coping are more likely to use professional help; individuals who do not use task coping are more likely to use instrumental services; subjects not receiving treatment were less likely to use services. There were no relationships between use of services and depression, date from diagnosis, number of symptoms, severity of symptoms, stage of disease, or gender. Forty percent of the subjects did not use any services and 13% indicated that at least one service they used was not useful. This data suggests that useful services are available but that efforts should be directed towards identifying the individuals who are more likely to use a specific service and removing barriers between patients and the services they require.

CH6

14 SHAKEN BABIES: A FOLLOW-UP STUDY OF THEIR FAMILIES. S. Mohammed* B.Sc., L. Macgill-Steven M.S.W., M. Mian M.D. F.R.C.P.(C). The Suspected Child Abuse and Neglect (S.C.A.N.) Program, The Hospital for Sick Children, Faculty of Medicine, University of Toronto, Canada, M5G 1X8. The Shaken Baby Syndrome (SBS) describes injuries incurred by infants due to severe shaking. This form of physical abuse of children results in acute brain hemorrhages (intracerebral, subdural or subarachnoid), retinal hemorrhages and bone fractures. A follow-up study of families was conducted on the 14 SBS cases referred to a hospital based child abuse program in 1993 and 1994 from the Pediatric Intensive Care Unit. The purpose was to determine the present environment of these families two to three years after abuse had been identified, and to examine physical abuse of children as both a health and social concern through an analysis of the determinants of health of these families. After the initial investigation of abuse by S.C.A.N., the long-term effects of intervention on family dynamics are unknown. In order to determine whether families continued in situations that put them at high risk for child abuse, we investigated the present health needs of the affected child, family living situation, personal and community supports of the caregivers, and legal proceedings in regards to the perpetrator. Qualitative information was obtained from unstructured phone interviews with parents, grand-parents, foster-parents, police officers and Children's Aid Society workers. Contact was made with at least one person involved with all 14 cases. We found that three of the children died shortly after admission, eight children had severe motor and cognitive disability, and all but one of the children had some permanent disabilities attributed to the incident. In 11 of the 14 cases, the living situation or custody arrangement of the family had changed and most families had moved several times. In cases where the mother's boyfriend was an alleged abuser, the mother remained supportive of the perpetrator. All the present caregivers described at least one person they turned to for support. Most families had multiple agencies involved in the care of their disabled child. In 8 cases charges were laid, in 6 the trials have concluded and the perpetrators have been found guilty. We concluded that although protection has been effective for most of the children (changes in custody, better caregiver support, perpetrators convicted), risk factors for physical abuse remained (chaotic family dynamics, multiple moves, no treatment for perpetrators). Important issues that arose from this study were the potentiating and compensatory mechanisms of abuse and prevention in families with a history of abuse, and the need for better follow-up of these families.

CH7

AN EVALUATION OF HEALTH CARE RESOURCE UTILIZATION IN THE MANAGEMENT OF HORMONE-RESISTANT PROSTATE CANCER. T. Neogi*, D.J. Bloomfield, I.F. Tannock. Medical Oncology, Princess Margaret Hospital, Faculty of Medicine, University of Toronto, Canada M5G 2M9.

Hormone-resistant prostate cancer is generally regarded as incurable, with an expected median survival of less than one year. This study seeks to evaluate health care resource utilization in the management of symptomatic hormone-resistant prostate cancer. Ten patients were randomly chosen from the Princess Margaret Hospital subset of patients entered in a multicentre study comparing chemotherapy versus best supportive care. This was a positive trial which demonstrated an improvement in patient-reported quality of life. All resources utilized from trial entry to end of the trial period, and through to death were recorded retrospectively by chart review on a relational database and costed. This allowed graphical depiction of the relative contribution to cost of various categories of care, such as inpatient and outpatient care, and different modalities of treatment. Provisional figures indicate the mean cost through to the end of life from the perspective of the health care system was in the range of approximately $20 000. Preliminary survey of results indicate that the predominant proportion of total expenses result from costs at the end of life, separate from the trial period. The majority of these expenditures were due to hospitalization. The extent of alternate care facilities available, such as home care and hospice care, and costs associated with such care were ascertained. Figures of cumulative costs plotted versus time illustrate a steeply rising increase in costs during the last months of life. The social and economic implications of these results suggest the need for exploration of optimal health care settings for the delivery of quality palliative medical and nursing care which integrates patient and family preferences.

CH8

PHYSICIANS' REFERRAL PRACTICES AND ATTITUDES REGARDING EARLY INTERVENTION. Alice Ordean, B.Sc.,* Elizabeth Thompson Ph.D., C. Psych, Wendy Roberts, MD., FRCPC, Child Development Clinic, HSC, Faculty of Medicine, University of Toronto, Canada, M5G 1X8

Early intervention (E.I.) programs are designed to serve infants and young children who are at risk for developmental delay. The aim of early treatment is to provide the affected child with opportunities to achieve maximal physical, intellectual and social development and to support their familes. Early treatment requires early identification and often involves a referral by the family physician or paediatrician.

This pilot study focused on referral practices and attitudes of physicians toward E.I. and examined communication patterns between physicians and early interventionists. Twenty-two physicians who had made a referral to an early intervention program in two regions of Ontario were administered a semi-structured questionnaire .

Physicians see facilitating child development as the primary role of E.I. programs. 95% of the physicians surveyed refer families to E.I. to promote their child's development while 77% also see E.I. helping to support families. 90% of those surveyed indicated they would usually refer a child who has an established developmental diagnosis to E.I.; however only 33% would refer children with a suspected developmental delay. Almost 1/2 of those who did not refer chose to wait and observe the childs development longer before referring. One third of the group stated they used the information provided by the early intervention programs in helping to confirm a diagnosis. 33% felt that the services in their region were not adequate citing lack of resources and lack of information about the programs as reasons for their concerns and difficulties with referring. Only 40 % of physicians learned about early intervention programs in their training in undergraduate or graduate medicine.

Improving physician/interventionist communication and physician education are important goals to ensure children and families receive the supports available in their community.

CH9

FINANCIAL IMPACT OF ADULTS WITH CONGENITAL HEART DISEASE ON HEALTH CARE DELIVERY

Ben Sivarajan*, Murray Krahn, David Harrison, Gary Webb, Samuel Siu. Toronto Congenital Cardiac Centre for Adults, The Toronto Hospital, Faculty of Medicine, University of Toronto

Many adults with congenital heart disease have hemodynamic and electrophysiologic residua and require serial monitoring at specialized centres. However, the direct cost of the serial monitoring of these patients has not been previously examined. We performed a retrospective study examining adults with congenital heart disease who were 18-20 yrs old in 1987 and were followed at the Toronto Congenital Centre for Adults from 1987 until 1992. The frequency and nature of their outpatient visits and tests were tabulated. Costs were then calculated using the OHIP schedule. **Results**: Seventy one adults with congenital heart disease (45% male) were followed for 163 patient years. The majority (73%) had undergone surgical procedures prior to age 18. Thirty seven patients (52%) were born with cyanotic heart disease. The entire group underwent 155 clinic visits, 154 ECGs, 63 CXRs, 56 echocardiograms, 23 exercise radionuclide angiograms, 22 Holters, 4 MRIs, 4 graded exercise tests, 2 lung scans, and 6 cardio-pulmonary studies. The total direct cost of outpatient care was $52971 or $325/patient year. Physician fees for clinic visits were responsible for 34% of the total cost. **Conclusions**: The average direct cost of providing outpatient follow-up to adults with congenital heart disease was $325/patient year. Physican fees for clinic visits were responsible for a significant proportion of the total cost.

EM1

DOES THE USE OF A TOPICAL LET SOLUTION PROVIDE SUFFICIENT ANALGESIA FOR THE REPAIR OF LACERATIONS IN THE EMERGENCY DEPARTMENT? A.J. Adler*, J. Eisen, I. Dubinsky. Department of Emergency Medicine, North York General Hospital, Faculty of Medicine, University of Toronto, Willowdale, Ontario, Canada M2K 1E1.

Topical anesthetic in the form of LET (lidocaine, epinephrine, tetracaine) solution has been used for repair of superficial lacerations. This randomized, double-blind study was designed to determine the effectiveness of LET in eliminating or reducing the pain involved in suturing superficial lacerations in adult patients. The effectiveness of LET in reducing the pain of local injection of additional anesthetic was also examined. Sixty adult patients with superficial lacerations were entered in the study with thirty receiving LET and thirty receiving placebo. Following application of the LET or placebo solution to the laceration, a visual analog pain scale was taken upon needle probing of the wound margin. If injection of local anesthetic was required, an additional pain scale was elicited. Pain scale values on needle probing were significantly reduced in the LET group versus the placebo group ($p<.05$). 17 of the 30 patients in the LET group did not require additional anesthetic, while all 30 patients in the placebo requested the need for additional local anesthetic. For those patients in the LET group that did receive additional local anesthetic, pain scale values were significantly reduced on injection when compared to the original pain scale values of the LET group on needle probing ($p<.001$) The mean reduction in pain scale values from needle probing to injection of the local anesthetic was significantly greater in the LET group compared to the placebo group ($p<.01$). No adverse effects were noted after the application of either LET or placebo solutions. Follow-up was accomplished in 54 of 60 patients with only one complication reported in the LET group. In conclusion, topical LET significantly decreased the pain involved in suturing superficial lacerations and reduced the need for local anesthetic. In addition, if local anesthetic was required, LET significantly reduced the pain upon injection.

EN1

GENETIC ENGINEERING OF AN INSULIN SECRETING *CHO* CELL LINE. M. Belyea*, A. Sun, E. Kintsurashvili. Department of Physiology, Faculty of Medicine, University of Toronto.

Somatic gene therapy is being considered in the treatment of hormone deficiency in insulin dependent diabetes mellitus (IDDM). This study hypothesizes that a recombinant cell line may be constructed to synthesize, store, and secrete insulin in response to glucose stimulation, and will sufficiently lower the blood glucose concentration in diabetic animals. A *CHO* cell line, derived from the Chinese hamster ovarian cell, was transfected with a mammalian expression vector carrying the human insulin gene (pCB6-hINS). Comparable amounts of insulin and proinsulin were released over 24 hours by the stable CHO-INS cells. Examination of cell extracts by radioimmunoassay (RIA) confirmed that insulin rather than proinsulin was preferentially being stored. Electron microscopy (EM) revealed large membrane-bound vacuoles, containing electron-dense material, which were not seen in control cells. The storage of insulin in the vacuoles will have to be confirmed by immunohistochemical analysis. A GLUT2-pREP7 expression vector was subcloned and transfected into the stable CHO-INS transfectants. Stable *CHO-INS-GLUT2* cells were isolated. Analysis of these stable cells by PCR, and further investigation into whether or not these cells will confer glucose stimulated insulin secretion are ongoing. If *CHO-INS-GLUT2* cells exhibit glucose stimulated insulin secretion, they will be microencapsulated to prevent immunorejection, and transplanted into diabetic animals for *in vivo* studies.

EN2

DOES MICROALBUMINURIA (MA) IN ADOLESCENTS WITH DIABETES (IDDM) PREDICT PROGRESSION OF DIABETIC NEPHROPATHY? D. Gorman*, E. Sochett, D. Daneman. Division of Endocrinology, The Hospital for Sick Children (HSC), Faculty of Medicine, University of Toronto, Canada M5G IX8.

In adults with IDDM of 10 to 20 years' duration, MA is highly predictive of progression to overt nephropathy. However, two recent studies that followed small numbers of adolescents with IDDM and MA for 3 years found much lower rates of progression and considerable rates of regression. Our objective was to describe the natural history of MA in adolescents with IDDM by following a larger cohort of patients for up to 11 years.

76 IDDM adolescents (44M:32F, mean age at baseline 13.63±1.69 years, IDDM duration at baseline 5.50±3.04 years) treated at the HSC Diabetes Clinic were identified as having had at least one study for MA over the past 11 years. Of these, 44 performed additional 24-hour urine collections in 1996 for measurement of albumin excretion rate (AER). Height, weight, BP, HbA1c and smoking history were recorded at the time of each AER measurement. Of the 47 without MA (AER<15 µg/min) on initial screening, 30 were again normal at final follow-up, while 17 progressed to MA (AER>15 µg/min). Of the 41 with MA on initial or subsequent screening, 12 had an increase in AER >50% of baseline, 14 had an AER that remained within ±50% of baseline, and 15 showed a decline in AER by >50%. Of these 15, 10 decreased into the nonMA range. Duration of follow-up (</> 5 years) did not substantially influence the results.

These data confirm the findings published recently that the presence of MA in adolescents with IDDM is not a strong predictor of progression towards overt nephropathy. It should be noted, however, that in the reported adult studies MA was first observed in the second decade of IDDM, whereas in our study it was first observed in the first decade of the disease. Further analysis is in progress to attempt to determine predictors of MA development and progression (e.g., baseline and changes in body size, BP, HbA1c, and smoking status).

EN3

NUTRIENT SIGNALS ARE MEDIATED BY THE VAGUS NERVE IN THE PROXIMAL-DISTAL REGULATION OF INTESTINAL PROGLUCAGON-DERIVED PEPTIDE (iPGDP) SECRETION. AS Rocca*[1] and PL Brubaker[1,2]. Department of [1]Physiology and [2]Medicine, Faculty of Medicine, University of Toronto, Canada.

Glucagon-like peptide-1 (GLP-1) is a member of the iPGDPs and is derived from proglucagon by post-translational processing in ileal L cells. GLP-1 is an exciting peptide seen as a potential treatment in type II diabetes. Its effects include increasing insulin secretion in a glucose-dependent fashion while suppressing the release of glucagon, as well as decreasing gastric acid secretion and gastric motility. It is well established that GLP-1 and the iPGDPs are released within 20 min of nutrient ingestion. Previous studies have demonstrated that the L cell is governed by a proximal-distal loop operating between the duodenum and ileum. The short response time of nutrient-induced iPGDP secretion suggests the existence of a neural component of the proximal-distal loop. This hypothesis was investigated in anesthetized rats and plasma levels of the iPGDPs were determined by RIA (n=5-6). To determine the role of the vagus nerve on basal iPGDP levels, the left cervical vagus nerve was transected. Basal iPGDP levels were reduced significantly by this procedure from 202±7 pg/ml to 110±8 pg/ml ($P<0.0001$). Corn oil placed into an isolated segment of duodenum resulted in an immediate rise in iPGDP levels with a peak increase of 192±46 pg/ml above basal ($P<0.05$). The response achieved when the gut was transected below the isolated duodenal segment was similar (183±65 pg/ml above control) indicating that the enteric nervous system is not involved in fat-stimulation of the proximal-distal loop. A bilateral subdiaphragmatic vagotomy performed prior to the administration of duodenal corn oil completely abolished the fat-induced rise and further reduced iPGDP levels to 150±33 pg/ml below basal ($P<0.05$). Furthemore, direct stimulation of the celiac vagal branch (20 Hz, 10 V, 15 min) increased iPGDP secretion by 71±13 pg/ml ($P<0.01$). This branch of the vagus serves the distal intestine which possesses a large number of L cells. Therefore, vagal mechanisms appear to mediate the proximal signal of nutrient ingestion to the distally-located L cells in order to control the secretion of GLP-1.

EPIDEMIOLOGY

EP1

DETERMINANTS OF OUTCOME OF ACUTE DIARRHEAL EPISODES IN CAIRO, EGYPT. R. Nahas*, AH Zidan, C. Bayliss. Department of Gastroenterology, Abu-el-Reeshe Pediatric Hospital, Cairo University, Egypt and University of Toronto, Canada.

Diarrheal dehydration is a major cause of infant and child mortality in Egypt. The WHO's National Control of Diarrheal Diseases Project (NCDDP) began in 1981 and led to widespread use of the WHO oral rehydration solution (ORS). Despite the NCDDP's success, much work remains to be done. Independent home ORS use and early feeding resumption are not universal, and inappropriate administration of antimicrobials and antidiarrheals by private physicians (for various reasons) is widespread.

A survey of 270 mothers of children (age < 5 years) with watery diarrhea (no blood or mucus) for<14 days was conducted at the rehydration clinic at the Abu el-Reeshe Pediatric Hospital during a four-week period in July of 1996. Mothers were asked about their awareness of the NCDDP campaign and ORS, care of their child at home (feeding practices and use of ORS), length of wait before seeking outside help, and first outside treatment (ORS, antimicrobials and/or antidiarrheals). Severity of dehydration was assessed clinically.

Of 270 mothers surveyed, 266 (98.5%) had seen the NCDDP television program. 240 (88.9%) knew how to use ORS correctly before seeking outside help, but only 141 of those (58.8%) used ORS for the current episode. 58 (21.5%) stopped feeding for ≥2 continuous days during the episode, and the mean waiting period before seeking outside help was 2.99 days. 53 of the 270 mothers seen were first-time mothers; 50 of them (94.3%) had seen the NCDDP program and 32 (58.5%) knew how to use ORS but only 9 (17.0%) did so. 30 (56.6%) stopped feeding for ≥2 continuous days, and the mean waiting period before seeking treatment was 3.57 days.

Of 270 children seen, 115 (42.6%) were first seen by private physicians. Only 11 physicians (9.6%) prescribed ORS alone, the recommended treatment for acute watery diarrhea. 61 (53.0%) prescribed antimicrobials or antidiarrheals in addition to ORS, while 43 (37.4%) prescribed these drugs alone. Of these 103 cases of overtreatment, 14.6% (15) presented with moderate or severe dehydration, compared with an overall incidence of 8.5% of such dehydration (23 of 270).

Knowledge of the NCDDP and ORS is widespread, but its home use is less common, as are early feeding practices. First-time mothers need the most education in these areas, and should be advised to seek outside help earlier. Private physicians still overprescribe antimicrobials and antidiarrheals, and this is associated with more severe dehydration.

EP2

CONTRASTING CARDIOVASCULAR AND CANCER MORTALITY RATES AMONG CHINESE, SOUTH ASIANS, WHITES IN CANADA. T Sheth*, M Nargundkar, K Chagani, S Anand, C Nair, S Yusuf. McMaster University, Hamilton and Statistics Canada, Ottawa.

There are limited data on variations in disease patterns among different ethnic groups in Canada. We studied cause-specific mortality rates among Whites (WH), Chinese (CH), and South Asians (SA) in Canada. Previous Canadian mortality studies have used country of birth to determine ethnic origin, a method which misclassifies as many as 20% of SA and CH cases. We therefore created a novel methodology based on unique surnames and reclassified 2.6 million deaths in the Canadian Mortality Data Base from 1979 to 1993. The sensitivity and specificity of our method, validated in SA, was 96% and 95%. Population of each ethnic group was obtained from Census data for 1981, 1986, and 1991. Age standardized mortality rates per 100,000 (age 35 to 74) were calculated.

Results:	WH	SA	CH
Ischemic Heart Disease (IHD)	208	232	72
Cerebrovascular Disease (CBVD)	42	43	45
Lung Cancer	85	16	53
Colorectal Cancer	31	7	23

Conclusion: Cause-specific mortality rates differ significantly among WH, CH, and SA. Since IHD and cancer often are the result of common exposures (eg smoking or high fat diet), the substantial variation seen in mortality from these diseases is remarkable and suggests many new hypotheses for future investigation. Further analyses, utilizing the method developed in this study, may be performed in different databases and among other ethnic groups. Elucidating ethnic variations in the principle causes of death will have major implications for health policy and disease prevention in Canada.

IMMUNOLOGY

IM1

BINDING SITES OF CYTOPLASMIC EFFECTORS TRAF 1,2 AND 3 ON CD30 AND OTHER MEMBERS OF THE TNF RECEPTOR SUPERFAMILY

L.M. Boucher*, L. Marengere, Y. Lu, S. Thukral, and T.W. Mak. Medical Biophysics Department, Princess Margaret Hospital, University of Toronto, Canada M5G 2C1.

CD30 is a cellular receptor found on activated lymphocytes that has brought much attention due to its presence in some lymphomas such as Hodgkin's and anaplastic large cell lymphomas. We have attempted to define a possible role for this receptor by using a yeast two hybrid genetic screen to identify molecular effectors which mediate CD30 signaling events. This has allowed us to identify predominantly three molecules known to be necessary in signaling by TNF receptor family members: TRAF 1, 2, and 3. We have further localized the binding to two sites located on the carboxy end of the CD30 intracellular tail using specific peptides to immunoprecipitate the TRAF molecules. Furthermore we show that similar sequences in the intracellular tails of TNF receptor p75 and CD40 have the same specificity in interacting with the TRAF molecules.

IM2

POST-TRANSPLANTATION LYMPHOPROLIFERATIVE DISORDERS FOLLOWING RENAL TRANSPLANT. F. M. Bovell*, S. Deodhare, D. F. Murray. Department of Pathology, St. Michael's Hospital, Faculty of Medicine, University of Toronto, Canada M5B 1W8.

We report on seven cases of post-transplantation lymphoproliferative disorders (PTLDs) occurring subsequent to renal transplantation. Slides of pathology specimens were examined histologically to determine morphological characteristics of the neoplasms. In addition, several monoclonal antibodies were used to delineate cell phenotypes and to detect the presence of intracellular Epstein-Barr virus, immunohistochemically. Three rare PTLD phenotypes were demonstrated. Case findings also allowed us to postulate a relationship between different accepted agents of pharmacological immunosuppression and the onset of PTLD.

IM3

ALLO-IMMUNIZATION IN THE CONTEXT OF AN HIV VACCINE STRATEGY Charles Dela Cruz*, John Chamberlain, Kelly MacDonald, and Brian Barber. Department of Immunology*, Hospital for Sick Children, Mt. Sinai Hospital, and Institute of Medical Sciences*, Faculty of Medicine*, University of Toronto, Ontario, Canada, M5S 1H8.

Recent literature has indicated that gene products of the major histocompatibility complex (MHC) are incorporated into the HIV-1 envelope as the virion buds from the host cell surface. Furthermore, antibodies specific for non-polymorphic determinants on either class I MHC or class II MHC are known to block infectivity of HIV virions *in vitro*. Studies in simian immunodeficiency virus (SIV) model in macaques has demonstrated strong correlation between protection from live SIV challenge and previous immunization with uninfected human cells and the presence of xenogeneic anti-MHC antibodies.

To better understand the relationship between anti-MHC immune responses and the ability to resist HIV infection, plasmid DNA immunization was used to invoke both B- and T-cell allo-immune responses to defined human class I MHC gene products in a transgenic mouse model system. cDNA expression vectors were constructed for use as plasmid DNA immunogens; one encoding HLA-A2 and the other HLA-B27. The fidelity of these class I genes were confirmed by DNA sequencing, and their ability to synthesize intact class I molecules were assessed by fluorescence-activated flow cytometry of transiently transfected COS-7 cells. Sets of mice transgenic for either HLA-A2 + human ß2-microglobulin (hß2m), or alternatively HLA-B27 + hß2m have been bred for intramuscular challenge with the different class I MHC expression vectors.

Both "syngeneic" and "allogeneic" immunizations (e.g. HLA-A2 expressing plasmid DNA into either HLA-A2 or HLA-B27 transgenics) were conducted to determine whether or not this type of immunization breaks tolerance and is able to induce strong antibody and T-cell responses specific for the class I MHC immunogen. These immunizations were also conducted with and without the parallel expression of co-stimulatory molecule B7-2. The ability of co-injected cytokine-expressing plasmids (specifically IL-12 and IL4) to enhance the different allo-immune responses were also assessed. Strong anti-MHC antibody responses, as determined by flow cytometry, were induced in the allogeneic immunizations, while no anti-self-MHC response was detected in the syngeneic immunizations. Summary of these and other results will be presented. Future studies will include determining the *in vitro* neutralizing potential of these allo-antibodies using virus grown in human cells expressing the MHC gene product in question.

IM4

ADRENERGIC STIMULATION INHIBITS NEUTROPHIL APOPTOSIS

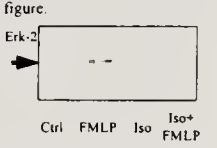
A. Jahromi*, R.W.G. Watson, J. Parodo, O.D. Rotstein, J.C. Marshall. Dept. of Surgery, CCRW2-861, The Toronto Hospital, University of Toronto, M5G 2C4.

The acute inflammatory response to an infectious stimulus is characterized by massive neutrophil (PMN) influx, a process that typically results in resolution of infection at the cost of bystander injury to host tissues. Termination of inflammation is believed to occur as a result of the activation of an endogenous cell death program known as apoptosis. Since adrenergic activation, a stimulus that elevates cAMP, accompanies significant systematic inflammation, we sought to determine the effects of the adrenergic agonist, isoproterenol (Iso), on the expression of PMN apoptosis. **Methods:** Human PMN ($1x10^6$), isolated from healthy volunteers, were incubated with Iso (20µg/mL), with or without: Timolol (40µg/mL) a β_2 adrenergic blocker, or H-89 (10µM), an inhibitor of PKA. Apoptosis was assessed by flow cytometric analysis of Propidium Iodide DNA staining and CD16 surface receptor expression, and by morphology (Mor). To confirm the adrenergic functional blockade by the above agents, respiratory burst activity in response to FMLP was assessed by Dihydrorhodamine 123. Erk-2 phosphorylation was assessed by western blotting using a mouse anti-human phosphorylated Erk-2 monoclonal Ab.

Results: The inhibitors Timolol and H-89 alone had no effect on PMN apoptosis.

Apoptosis	Mor (18 hrs)	PI (18hrs)	CD16(6 hrs)	ROI
Ctrl	43.3± 7.9	31.4±3.5	27.4±15.5	88.4±2.7
Iso	21.9± 3.2*	15.5±4.4*	15.5±4.9*	28.3±6.6*
Iso + Timolol	36.3±3.6#	26.4±2.1#	25.1±2.4#	83.8±2.7#
Iso + H-89	-	20.9±2.8	27.5±4.9	-

figure.



Results = mean±SD. *$p<0.05$ vs Ctrl, #$p<0.05$ vs Iso, ANOVA.

Iso delayed PMN apoptosis and inhibited FMLP induced respiratory burst, these effects were blocked by Timolol and H-89. Similar delay in apoptosis was obtained using the adenylyl cyclase activator, forskolin. Iso reduction of FMLP induced respiratory burst is associated with inhibition of Erk-2 phosphorylation (figure). **Conclusion:** The adrenergic agonist, isoproterenol, inhibits PMN apoptosis through a pathway involving the β_2 adrenergic receptor, and PKA activation via elevated cellular cAMP. The adrenergic response is both a novel mechanism and a potential therapeutic target, for the modulation of inflammation.

IM5

HYDROGEN PEROXIDE PRODUCTION FROM NEUTROPHILS FOLLOWING AAA REPAIR. Paul Williams* MSc, Thomas Lindsay MD MSc Division of Vascular Surgery, Toronto Hospital, Faculty of Medicine, University of Toronto, Canada M5G 1X8.

This laboratory has previously shown that the period of lower torso ischemia during Abdominal Aortic Aneurysm (AAA) repair is associated with enhanced oxidative activity of neutrophils, reflecting a systemic inflammatory response possibly contributing to significant organ dysfunction often seen in the postoperative period. Neutrophil oxidative activity was measured via chemiluminescence (CL), a process using luminescent dyes readily oxidized by reactive oxidants. CL has been used as an index of hypochlorous acid production by neutrophil myeloperoxidase. The benefits of CL are that it is performed using small amounts of whole blood, and measures intracellular as well as extracellular oxidant production. However, the CL technique measures the photon emission byproduct of the oxygenation reaction, and may be subject to interference from other oxygenation reactions.

The purpose of this project was to develop a method to directly measure H_2O_2, an intermediate oxidant generated by neutrophils, and to correlate neutrophil H_2O_2 production with CL results in elective AAA patients. The assay developed measures the oxidation of scopoletin by H_2O_2 in the presence of horseradish peroxidase. Oxidation of scopoletin reduces its fluorescence directly proportional to the amount of H_2O_2 in the extracellular fluid. Quantitation is achieved using a linear standard curve created from exogenous H_2O_2 concentrations. Preliminary results have consistently shown significant H_2O_2 production in activated normal human neutrophils, and correspond well with values reported in the literature. This assay, however, requires purified neutrophils and is more time consuming than CL. Data from elective AAA patients will be displayed at the presentation.

This method of direct measurement of H_2O_2 production in human neutrophils is a more widely accepted measure of oxidant production, and will provide an important correlation with results from the simpler CL assay.

IN1

AN OUTBREAK OF *STENOTROPHOMONAS MALTOPHILIA* (Sm) BACTERAEMIA IN HEMATOLOGY-ONCOLOGY PATIENTS AT THE TORONTO HOSPITAL (TTH). S. Fung*, E. Choi, J. Louvaris, A. Humar, H. Dedier, I. Campbell, J. Strauss, M. Garcia, P. Savage, J. Brunton, J. Conly. Department of Microbiology and Nursing, The Toronto Hospital, University of Toronto, Toronto, Canada M5G 2C4.

Infections caused by *Stenotrophomonas maltophilia* (Sm) have been increasingly recognized in patients with compromised host defences. Epidemiologic surveillance of blood culture isolates at TTH between identical 5 month periods of 1994 and 1995 revealed an increase from 3/47 (6%) to 19/61 (31%) gram-negative bacteremias due to Sm in patients from the Hematology-Oncology ward. Epidemiologic investigations revealed no common source to explain the increase and molecular subtyping of isolates using pulsed-field gel electrophoresis (PFGE) and random primer polymerase chain reaction (RP-PCR) showed no identical macrorestriction profiles in any of the isolates. Forty perirectal screening swabs from 20 patients using a selective imipenem agar revealed no colonization at these sites. Environmental screening cultures from sinks, drains, refrigerators, multidose heparin and saline vials from both inpatient and outpatient areas revealed only 2 isolates, both of which were dissimilar to the clinical isolates. A case-control study examining over 25 potential risk factors for bacteremia was undertaken with 2 contemporaneous controls chosen (1 bacteremic, 1 non-bacteremic) for each case. For Sm vs bacteremic controls the number of hospitalizations (4.8 v 1.7), 7 or > d of ciprofloxacin usage, 4 or > visits to the outpatient clinic and polymicrobial bacteremia were all significantly associated with Sm infection on univariate analysis. The presence of polymicrobial bacteremia was independently associated with Sm bacteremia on logistic regression analysis. For Sm vs non-bacteremic controls, central line duration, length of stay and the use of tobramycin/cefazolin were additional associated factors. Mortality from bacteremia due to Sm was significantly (p=.04) higher than non-bacteremic controls. These findings suggested a line-related source potentially related to visits to the outpatient area and contamination with "waterborne" pathogens. Following a complete review of central line care practices in the outpatient areas, the incidence of Sm bacteremias in this population has dramatically decreased with only 2 bacteremias reported over the ensuing 10 months.

IN2

INFLUENCE OF HIV INFECTION ON THE NATURAL HISTORY AND SEROLOGY OF HEPATITIS C INFECTION

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Infection with hepatitis C (HCV) is relatively common in HIV-infected patients because the modes of transmission for the two viruses are similar. Although studies have shown that the presence of hepatotropic viruses does not have an effect on progression of HIV to AIDS, there is conflicting evidence as to the effect that HIV has on the natural history and serology of HCV infection. This investigation determined the prevalence and demographics of infection with HCV in the HIV(+) population at the Toronto Hospital Immunodeficiency Clinic. We also correlated the presence of liver disease with immune status as determined by CD4 levels, and viral loads of HIV and HCV. A retrospective review was done on 287 randomly selected patient charts. Information was extracted on HIV and HCV risk factors, gender, age, first known HIV sero-positivity, CD4 values, liver function tests, relevant physical exam abdominal findings, hepatic investigations, history of opportunistic infections, and history of use of potentially hepatotoxic agents. Serum was collected and subjected to quantitative PCR to determine HIV and HCV viral loads from: all HCV Ab(+) individuals, HCV Ab(-) individuals with < 200 CD4 cells/ml at the time of HCV testing, and from HCV Ab(-) individuals with liver disease. The findings were subjected to multivariate analysis. Our results developed a clinical profile of HIV(+)/HCV(+) individuals and demonstrated that there are several significant effects that HIV infection imposes upon the course of HCV infection.

IN3

THE SEQUENCE OF A GENE HOMOLOGOUS TO *HGL2* OF *ENTAMOEBA HISTOLYTICA* THAT IS PRESENT AND EXPRESSED IN *E.DISPAR*.

Dylan R. Pillai[†], Dawn Britten*, John P. Ackers*, Jonathan J. Ravdin[‡] and Kevin C. Kain[†¶]

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Adherence and cytolysis of target cells by the pathogenic protozoan *Entamoeba histolytica* is mediated by the Gal/GalNAc-specific lectin. The functional 170-kDa heavy subunit is encoded by at least five members of a gene family (*hgl1-5*). By using a PCR-based strategy, a homologous gene from the non-pathogenic protozoan *Entamoeba dispar* (*SAW 760*) was amplified from genomic DNA, cloned, and sequenced. The DNA sequence identified an open-reading frame of 3768 nucleotides which maintains 85% identity to *hgl2* at the predicted amino acid level, and 81% identity to *hgl1* and *hgl3*. All 97 cysteines in the putative carbohydrate binding domain of the Gal/GalNAc lectin are conserved. However, only 5 of 9 potential *N*-linked glycosylation sites are retained in the *E.dispar* homologue (*dhgl2*). Three potential tyrosine-phosphorylation sites in the cytoplasmic tail remain conserved. CD59 homology, implicated in complement evasion conferred by the lectin, is also present in *dhgl2*. Southern blot hybridization and RT-PCR confirmed that *dhgl2* was specific to *E.dispar* genomic DNA and also expressed in this protozoan. A PCR-RFLP strategy, predicated on the presence of a unique *Hind*III site in *dhgl2* but absent from all known members of the *hgl* gene family in *E.histolytica*, may be a useful diagnostic tool in distinguishing *E.dispar* from *E.histolytica*.

ME1

USING THEORIES OF ANIMATION AND COLOUR IN THE VISUALIZATION OF A PHYSIOLOGICAL CONCEPT: LYMPHATIC DRAINAGE OF CEREBROSPINAL FLUID (CSF). K. Chorney*, M. G. Johnston, L. Wilson-Pauwels, M. Boulton, and N. Woolridge. Division of Biomedical Communications, Faculty of Medicine, University of Toronto, Canada, M5S 1A8

The significance of the lymphatic contribution to drainage of the CSF has been measured in sheep and this concept is now poised to gain wide acceptance in the biomedical community. The concept is a complex one comprising anatomical, physiological, and mathematical factors. Visualization is needed to assist researchers and their audiences in presentation of this concept.

We are developing a visualization of this concept, incorporating theories of animation and colour. Animation is appropriate for the visual communication of a physiological system that involves flow through communicating fluid compartments, because animation presents the system in its natural state -- in motion. Colour-coding is effective for summarizing and clarifying complex information. Combining colour coding and animation such that colours may be seen flowing and blending is a uniquely appropriate means of clarifying this concept. This approach has not been undertaken before in the presentation of such a concept.

The visualization takes the form of a hypermedia module containing 2- and 3-dimensional animation. The target audience includes the biomedical research community, practitioners and residents in the neurosciences, and senior medical students.

The project involves cross-disciplinary research into the biomedical subject, the effectiveness of graphics and animation for communicating medical subject matter, animation technique, film language, and theories of art.

The development of the module is based on formative feedback from post-graduate level researchers in the neurosciences. Artistic and instructional design decisions are made according to this feedback and theories of animation, colour, and design. These principles are applied to the presentation of a basic science topic.

This research project is due to be completed in 1997.

ME2

CLERKSHIP TRAINING AND MEDICAL STUDENT ATTITUDES REGARDING EFFECTIVE COLLABORATION WITH COMMUNITY AGENCIES. L.K. Hicks*, D. Wasylenki. Faculty of Medicine, University of Toronto, Canada M5G 1X8.

In an environment of decreasing hospital stays with a consequent shift of health care into the community, a physicians' ability to interact effectively with community health agencies (CHA's) is extremely important. Previous studies have reported that physician collaboration with CHA's has been an area of disappointment for the public and insecurity for some members of the the profession. These short-comings could be addressed through medical education.

The objective of this study was to determine whether 3rd and 4th year clerks in the Faculty of Medicine at the University of Toronto are taught to collaborate with resources outside of the hospital, and whether this teaching is effective. A short survey which assessed attitudes, knowledge and skills in this area, and clerks' perceptions of their teachers' attitudes, was distributed to 240 clerks. One-hundred and fifty-six surveys were completed. Eighty-five percent of clerks believe that it is important to incorporate CHA's into patient care. In contrast, clerks' believe that only 54% of teachers think the same. A majority of clerks never, or only rarely, received information addressing collaboration with CHA's. The proportion of clerks who frequently observed a physician referring patients to a CHA (28%) was approximately equal to the proportion who observed a non-physician (social worker etc.) performing the same task (30%). Despite the relative infrequency with which collaboration with CHA's was addressed, 50% of clerks felt they received adequate training in this area, and 63% felt prepared to help patients gain access to CHA's.

There are three possible explanations for this apparent contradiction: (1) involving CHA's in patient care is common sense and does not need to be explicitly taught; (2) implicit education is occuring which is not reflected in these results (3) some clerks over-estimate their competence in this area. Analysis of the data and of student comments suggests that (2) and (3) are the most likely explanations for high confidence levels in the absence of explicit teaching.

ME3

PATIENT-CENTRED MEDICINE IN A REFORMED M.D. CURRICULUM: DOES IT MAKE A DIFFERENCE TO MEDICAL STUDENTS?

D. Robertson. Faculty of Medicine, University of Toronto, Canada M5S 1A8; and Department of Applied Social Studies, Faculty of Social Studies, University of Oxford, England OX1 2ER.

This ethnographic study, the first phase of which is covered here, aims to explore the perceptions of medical students about patient-centred medicine in the new M.D. curriculum put into effect in 1992 by the University of Toronto Faculty of Medicine. Executed through nine focus groups with 48 pre-clerkship medical students, the study indicates that most such students—albeit to varying degrees—endorsed the patient-centred aspects of the new curriculum. Most students believed these aspects were important parts of their education, relevant to their current and future practice with patients. The degree to which students' views were congruent with the faculty's enunciation of patient-centred medicine, however, differed widely. Students also expressed a wide range of opinions about how effectively the curriculum teaches patient-centred medicine; individual instructors were the most often-cited determinant of the effectiveness of patient-centred teaching. A large minority of students stated that patient-centred learning can aid biomedical learning; another large minority stated that patient-centred learning tends to detract from biomedical learning. These are the results of the first phase of a four-phase study, and should therefore be treated as preliminary.

ME4

A NOVEL STUDENT-INITIATED ELECTIVE: EVALUATION OF TEACHING MODALITIES IN PSYCHIATRY & PSYCHOTHERAPY. B. Taylor*,K. Rhee, M. Paré The Medical Clinic for Person-Centred Psychotherapy, Toronto, Canada M2N 3A9

A novel elective for medical students has been established for the purpose of educating medical students in the disciplines of psychiatry and primary care medical psychotherapy. The basis for this student initiated elective was the recognized lack of exposure to these disciplines in the early years of medical school training, (1). Furthermore, the elective served as a pilot study in evaluating the effectiveness of different modalities in teaching primary care medical psychotherapy. Indeed, studies have shown that there is a need for more effective teaching techniques for medical students (2). Various topics in psychotherapy and psychiatry were presented with a variety of teaching modalities. Among the issues covered in this elective were: depression, manic-depression, schizophrenia, recognition of boundary issues in psychotherapy, doctor-patient communication, marital problems, sexual dysfunctions, personality disorders and the proper use of Prime-MD as a tool for primary care evaluation of mental disorders. The physicians that were recruited to teach utilized an array of educational tools ranging from didactic seminars and open discussions to role play and video analysis. The students were also able to observe psychotherapy sessions between the physician and patients either in individual or group therapy. These different modalities were evaluated using a scale from 1 to 10 (10 being "excellent", 5 being "satisfactory" and 1 being "poor") to evaluate the effectiveness of each. The scores for each modality ranged between 6.2 and 9.0. The results were as follows: patient interview with discussion, 9.0; video with analysis, 8.5; psychoeducational game play, 8.0, interactive interview, 7.5; role play, 6.5; didactic seminar, 6.0. The overall subjective experience of the elective was deemed outstanding, as was the educational experience. Several general trends can be noted from this data. First, modalities that were closer to the clinical setting, such as the psychotherapeutic interview rated higher. Second, novel methods such as video analysis and psychoeducational game play were well received. Third, the didactic seminar which had the lowest rating, was an ineffectual educational tool relative to the other modalities. 1. Paré, Michael & Cooper, H.M.: "Examining GP Psychotherapy in Ontario", OMR, Feb.1996. 2. Robertson M.: "Psychotherapy Education and Training: An Integrative Perspective", IUP, 1995. Madison, Conn. (The authors acknowledge the educational grant given by Lundbeck Canada, Inc.)

MG1

The Philandering Retinoblastoma Protein and its Multiple Affinities.

David DiCiommo[1,2,3], Brenda Gallie[2,3] and Rod Bremner[3].

[1]MD/PhD Programme, [2]Department of Molecular and Medical Genetics, [3]Eye Research Institute of Canada, Faculty of Medicine, University of Toronto, Canada.

The retinoblastoma protein (pRB) is a tumour suppresser. It acts as a transcriptional repressor by binding and inhibiting the activity of the E2F family of transcriptional activators. By blocking E2F, pRB effectively represses the expression of several genes necessary for DNA synthesis. This ability to repress transcription suggests that pRB is brought down to DNA through an E2F-1/DP-1 dimer complex dependent manner. In solution, pRB cannot block transcription factors it binds weakly. However, a model for the ability of pRB to quench transcription is that once tethered to the E2 promoter site, pRB is thought to block the activation of adjacent transcription factors via direct interactions by forming a tri-molecular complex. Although pRB and its weak binding partners do not interact in solution, once pRB is attached to DNA this insubstantial interaction is sufficient to block activation of gene transcription. My goal is the precise determination of rate equations and affinity measurements for pRB and its binding partners to understand the role of these weak protein-protein interactions in mediating transcription. The first phase in biophysical characterization of protein-protein interactions is to obtain homogenous protein samples. This involves obtaining >95% purified, soluble and native proteins. Presented are the purification protocols for these three molecules: pRB, pDP-1 and pE2F-1. GST-RB, GST-E2F-1 and GST-DP-1 were purified by affinity and ion exchange chromatographies. The GST moiety was removed from GST-E2F-1 and GST-DP-1 using factor Xa and thrombin enzymes, respectively, and furthered purified by ion exchange chromatography. The first stage in the affinity analysis involves transcription factors that pRB binds strongly. Models are presented for "real-time" binding rates that quantitatively measure the interactions between pRB and these transcription factors, both free and in the presence of their DNA binding sites using the BIAcore™ biosensor technology.

MG2

IN VITRO MODEL OF RETROVIRAL- MEDIATED GENE TRANSFER AND EXPRESSION TO CORRECT PURINE NUCLEOSIDE PHOPHORYLASE (PNP) DEFICIENCY IN HUMAN LYMPHOCYTES. E. Hait*, X. Wu, C. Roifman, J. Ellis. Department of Genetics, The Hospital for Sick Children, Faculty of Medicine, University of Toronto, Canada.

Purine nucleoside phosphorylase (PNP; EC 2.4.2.1) deficiency is a rare autosomal recessive disease associated with a fatal T cell immundeficiency in children. It has been proposed as a candidate for gene therapy by introduction of a functional PNP gene into either T lymphocytes or, preferably, into more primitive progenitor cells in the bone marrow. As an *in vitro* model of gene therapy for PNP deficiency, retroviral-mediated PNP gene transfer into human lymphocyte cell lines was attempted using a 3.5 kb retroviral construct called BGT30 that also contains a selectable neo gene. PA317 amphotropic packaging cells were transfected with BGT30, selected for with G418, and individual cell clones isolated. Cell clones producing high titre were identified by viral RNA Dot Blots and G418 selection on RATII cells. High titre BGT30 virus was then used to infect Jurkat cells (a PNP^+ T cell line) and EbV cells (a PNP^- B cell line). DNA, RNA, and protein from the infected Jurkat and EbV cells were then extracted for analysis. Southern blots confirmed viral intactness. Northern Blots indicated that PNP mRNA was being synthesized from the BGT30 vector. Protein assays are currently in progress. Enhancement of gene transfer is being attempted in two ways. Firstly, in an attempt to improve the vector, these experiments are being repeated using BGT31, an identical vector in which the neo gene has been deleted. Secondly, in an attempt to improve transfer, a second packaging cell line, PG13, will be infected. PG13 has been shown to produce virus with increased ability to infect hematopoietic stem cells. The preliminary results suggest that BGT30 may be a suitable vector for retroviral-mediated gene transfer as therapy for PNP deficiency.

MG3

HSP83 mRNA LOCALIZATION AND CLONING OF HSP83 3'UTR IN *DROSOPHILA VIRILIS*

A. D. Shearing*, A. Bashirullah, and H. Lipshitz. Department of Endocrinology, Hospital for Sick Children, 555 University Ave., Toronto, Ontario.

Heat Shock Protein 83 (Hsp83) was identified in a screen for mRNA transcripts with posterior subcellular localization in the developing *Drosophila melanogaster* embryo. We have since shown that this posterior localization is achieved by a novel mechanism involving generalized degradation and posterior protection of the ubiquitously expressed maternal transcript. Posterior protection has been shown to be directed by sequences in the 3'UTR of the Hsp83 transcript. In situ analysis has revealed an identical pattern of Hsp83 localization in the *Drosophila virilis* embryo. Although, *Drosophila melanogaster* and *Drosophila virilis* are approximately 60 million years divergent, both contain a single Hsp83 gene with >90% open reading frame sequence identity within the known sequence. The 3' ORF and UTR of *Drosophila virilis* Hsp83 have not been cloned. We have isolated by PCR, and partially sequenced, a clone containing the remaining 3' ORF and UTR from a *Drosophila virilis* cDNA library. The 3'UTR sequence will be compared with the *Drosophila melanogaster* sequence in an attempt to identify conserved putative subcellular localization signals. In addition, chimeric Hsp83 genes containing the *Drosophila melanogaster* 5'UTR and ORF and the *Drosophila virilis* 3'UTR will be used to rescue Hsp83 mutant flies in order to demonstrate conservation of Hsp83 3'UTR function. These investigations will help to further elucidate the molecular processes through which this novel Hsp83 subcellular localization is achieved.

NE1

MINIMUM URINE FLOW RATE DURING WATER DEPRIVATION: IMPORTANCE OF THE PERMEABILITY OF UREA IN THE INNER MEDULLA. I. Lenga*, R.Y. Cheung, M. Gowrishankar, S. Cheema-Dhali, M.L. Halperin. Renal Division, St. Michael's Hospital, Faculty of Medicine, University of Toronto, Canada M5B 1A6.

In the presence of ADH, urea is considered to be freely permeable across the inner medullary collecting duct, and thus ineffective at generating an osmotic gradient. Yet, urine flow rates are maintained even when urinary solutes are almost exclusively urea. This study evaluated if altering the rate of sodium chloride excretion during antidiuresis would influence urea's effectiveness as a urinary osmole.

Methods: 14 normal humans were water deprived for 12-16 hours and given 0.2-0.3 μg/kg of DDAVP, an ADH analogue. 6 subjects had high rates of electrolyte excretion induced by thiazide diuretics. 8 subjects had reduced electrolyte excretions induced by a low salt diet and prior furosemide diuresis. Urine was collected before and after consumption of 3mmol/kg of urea and examined for volume, total osmolality, and concentrations of electrolytes, urea, and creatinine.

Results: In the subjects with high salt excretion rates, urine flow rate was directly proportional to the "non-urea" osmole (i.e. electrolytes) excretion rate and there was no change in the osmolality of these solutes despite large changes in their excretion rates. Following the urea load, there was no change in urine flow rate, "non-urea" osmolality, or "non-urea" osmole excretion rates. The only changes in the urine were a doubling of urea concentrations (142±30 mM to 298±33 mM, $p<0.01$), urea excretion rates, and urine osmolality. In contrast, in the low salt protocol, flow rate increased almost 3-fold after the urea load (0.36±0.05 to 0.91±0.13 ml/min, $p<0.01$), with no increase in urea concentration despite a large increase in urea excretion. While urine osmolality was unchanged, the total "non-urea" osmolality fell below that in plasma.

Conclusions: Increased urea excretion is associated with a rise in urinary urea concentration when electrolyte excretion rate is high, but a rise in the minimum flow rate when electrolyte excretion rate is low. Thus urea's effectiveness in generating an osmotic gradient is dependent on the rate of electrolyte excretion.

NS1

DEXAMETHASONE-INDUCED NEUROPROTECTIVE CHANGES IN AN ANIMAL MODEL OF PERINATAL HYPOXIA-ISCHEMIA: A POSSIBLE ROLE FOR APOPTOSIS-RELATED GENES. K. J. Bernard*, G. M. Zhang, G. Cottrell, W. M. Burnham, J. H. Eubanks. Depts. of Pharmacology and Neurosurgery, Playfair Neuroscience Unit, The Toronto Western Hospital, Faculty of Medicine, University of Toronto, Canada, M5T 2S8.

Perinatal hypoxia-ischemia often leads to neurological dysfunction or cell death manifest as cerebral palsy, mental retardation and forms of intractable epilepsy. Dexamethasone, a synthetic corticosteroid, has been demonstrated to provide a dramatic neuroprotective effect in animal models of perinatal hypoxia-ischemia, but only if administration is between 4 and 24 hours before the insult. Since steroids are involved in the regulation of gene transcription, it is hypothesized that the neuroprotective effects of dexamethasone involve alterations in gene expression, such as the induction of anti-apoptotic genes, or the suppression of pro-apoptotic genes, thus resulting in neuroprotection. This study examined the potential induction of pro-apoptotic genes such as Bax and the suppression of anti-apoptotic genes such as Bcl-x by hypoxia-ischemia, and the antagonism of these processes by dexamethasone.

Our results demonstrate that hypoxia-ischemia induces the expression of Bax protein and decreases the mRNA expression levels of Bcl-x. Dexamethasone unexpectedly induces Bax protein, causes no apparent change in the level of Bcl-x and was antagonized by RU-486. These results suggest that the neuroprotective effects mediated by dexamethasone are not due to the induction of Bcl-x nor the down-regulation of Bax, but that other mechanisms are involved. Since dexamethasone has no neuroprotective effect in the adult, we speculate that factors present only in the neonate mediate neuroprotection. Identification of such factors may prove valuable in establishing a mechanism by which neuroprotection can be exogenously supplied to the adult brain.

NS2

SELECTIVE INJURY OF HUMAN OLIGODENDROCYTES MEDIATED BY MEMBERS OF THE TNF RECEPTOR SUPERFAMILY. Sameer D. D'Souza* and Jack P. Antel. Neuroimmunology Unit, Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Quebec H3A 2B4.

Using dissociated enriched cultures of human adult and fetal central nervous system (CNS) neural cell populations, we investigated whether differences in expression, or activation, of the TNF superfamily of receptors (TNFR and fas) could account for the selective injury of oligodendrocytes (OLs), as occurs in the human demyelinating disease, multiple sclerosis (MS). Apoptotic injury was assessed in terms of DNA and nuclear fragmentation, using the TUNEL and propidium iodide staining techniques, respectively; lytic injury was assessed by lactate dehydrogenase release. Although all the neural cells tested expressed TNF receptors, TNFα and β were selectively cytotoxic only to the OLs, inducing apoptosis over a 96 hr period. Ciliary neurotrophic factor (CNTF) protected the OLs from TNF-induced apoptosis. Amongst adult glial cells, fas was selectively expressed on OLs both *in vitro* and in MS plaques. Ligation of this receptor with the anti-fas antibody, M3 (Immunex Corp.) induced apoptosis-independent lysis in the OLs *in vitro* within 24 hr. CNTF did not protect OLs from fas lytic injury. Fetal astrocytes did however express fas, but were resistant to injury upon fas ligation with M3. Our results indicate that differences in receptor expression and susceptibility to a common immune mediator may potentially contribute to selective target cell injury in the CNS. Strategies aimed at protecting neural cells from immune-mediated injury may have to take into account the nature of the injury response (apoptosis vs. lysis) induced in the target cell.

NS3

FRONTAL EEG AROUSALS ARE ASSOCIATED WITH INCREASED HEART RATE SIMILAR TO CONVENTIONAL AROUSALS. *D.T. Farkas*, E.B. O'Malley, R.G. Norman, J.A. Walsleben, D.M. Rapoport.* Pulmonary and Critical Care Medicine, Department Medicine, New York University Medical Center, NY, NY 10016.

Upper airway muscle tone decreases at sleep onset and can lead to altered respiratory function ranging from incomplete obstruction (flow limitation) to complete obstructive apnea (absence of flow). Virtually all obstructive events are associated with fragmented sleep (Guilleminault ARRD 1976; 27:465-484) and increased heart rate (Pitson et al, Clin Sci 1994; 87:269-273). While most terminate with cortical EEG arousal as well, some 20% do not (Carley et al, ARRD 1988; 137:A60). However, we have recently shown that most of these events do terminate with an EEG arousal that is missed by the conventional leads but seen in frontal leads (O'Malley et al, Sleep Res. 1996; 25:287). This occurred most often after flow limitation events (O'Malley et al, AJRCCM 1996; 153:A568). The present study sought to determine whether frontal EEG arousals following flow limitation events are associated with heart rate changes similar to those seen with conventional EEG arousals. **Methods:** In 8 patients (5M, 3F, 43.4 ± 9.3 yr) with untreated sleep-disordered breathing (26.3 ± 18.4 apneas or hypopneas per hr sleep) ASDA arousal criteria was applied to both conventional and frontal EEG leads at the termination of flow limited events. ECG was monitored with a modified Lead II. The mean R-R interval was measured in the five beats preceding an arousal (PRE HR) and compared to the five beats following the arousal (POST HR). During long runs (>30 sec) of continuous flow limitation, random ten beat intervals were chosen as controls and analyzed in the same manner. In all cases the mean R-R interval was converted to the corresponding HR prior to statistical analysis. **Results:** Heart rate increased significantly during frontal EEG arousals and was similar in magnitude to the increase during conventional arousals. **Conclusions:** These findings suggest that frontal EEG arousals have similar autonomic consequences and fragment sleep like conventional arousals. This may help explain the daytime sleepiness that accompanies subtle breathing disorders of sleep such as the Upper Airway Resistance Syndrome.

	N	PRE HR	POST HR	%-Δ	p
Frontal	57	65.0±3.1	70.5±2.9	8.5 %	<0.0001
Conv.	40	64.1±3.5	69.7±3.2	8.7 %	<0.0001
Control	40	63.8±3.3	64.3±3.3	0.8 %	NS

NS4

EFFECT OF AUDITORY STIMULUS PARAMETERS ON SOUND LOCALIZATION IN NORMAL LISTENERS. C.G. Gujrathi *, S.M. Abel. Hearing Research Laboratory, Samuel Lunenfeld Research Institute, Mount Sinai Hospital.

This research assessed the ability of human listeners to localize one-third octave and broad noise bands. The effects of stimulus frequency (500 Hz, 4000 Hz, and broadband), stimulus rise decay time (10 vs. 50 ms) and stimulus duration (50, 300, and 380 ms) were investigated using a set of six loudspeakers surrounding the subject in the horizontal plane. The subjects were twelve experimentally naive males and females, with screened normal hearing. Sound localization was assessed by means of a forced-choice speaker identification paradigm. Subjects achieved 100% correct in localizing broadband noise, regardless of duration/rise decay. Scores were significantly lower for the one-third octave bands. There was no difference due to frequency for the three longer durations. For the short duration/short rise decay, a relative improvement was observed for the low frequency and a decrement for the high frequency. There were also strong azimuthal (angular) effects, related to frequency dependent front/back confusions. The results showed a strong frontal bias at 500 Hz and a rearward perceptual bias at 4000 Hz which were reflected in the azimuthal accuracy score. These outcomes helped to further our understanding of the utilization of binaural and spectral cues for directional hearing. In addition, the data suggested limitations for the operation of the precedence effect (law of first wavefront) in sound localization.

NU1

INVESTIGATION OF LIFESTYLE AND DIETARY HABITS OF CHINESE WOMEN IN TORONTO WITH RESPECT TO RISK FACTORS FOR BREAST CANCER, CARDIOVASCULAR DISEASE AND OSTEOPOROSIS. Dini Hui*, Dr. Christine Derzko, MD. Department of OB/GYN, St. Michael's Hospital, Faculty of Medicine, University of Toronto, Canada.

Preventative measures against disease and poor health can forstall mortality and morbidity in people of all ages, including women. Chinese people in Western countries exhibit higher rates of many chronic diseases than those in Asia, thus environmental factors play a role in the incidence of these diseases. There is a lack, however, of data pertaining to Chinese women in Western countries, thus it is important to investigate environmental and lifestyle factors with respect to CVD, breast cancer, and osteoporosis risk factors in this population. This report describes BMI, dietary intakes, smoking and exercise habits, and alcohol consumption of recent immigrant Chinese women residing in Toronto. Comparisons to a control population, recommended guidelines (RNI) and NHANESIII populations are made.

72 immigrant Chinese women in Toronto aged 35-55 years, and 67 women from a mixed population simulating Toronto's multiethnic community completed a written questionnaire prepared to investigate the factors of interest.

Phytoestrogen intakes averaged 21.6 mg/day in the Chinese population, whereas no control subjects consumed soy products. BMI were significantly lower in Chinese women. The Chinese diet was significantly lower in most nutrients than the control population, with low intakes with respect to RNIs with possible negative health implications. Regular exercise habits were not prominent in the Chinese.

Significant differences exist between Chinese and Western populations with respect to lifestyle and dietary habits. Further investigation is essential. The results of this study should be used to promote disease prevention. Chinese women need to be alerted to risks imposed on their health by their lifestyles and should then act accordingly.

NU2

EFFECTS OF ALTERING WHEAT BRAN PARTICLE SIZE ON BLOOD LIPIDS. TPP Ransom*, N Tariq, DJA Jenkins. Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Canada M5S 3E2.

Wheat bran is a high source of insoluble fibre which is generally accepted as being lipid neutral. Coarse-ground wheat bran (1400 microns) has a significant laxative effect while fine-ground wheat bran (400 microns) has little. We are interested whether particle size also effects lipid neutrality. To study this, 46 subjects (17 pre-menopausal females, 10 post-menopausal females and 19 males) were placed on a 2-week randomized cross-over study with a 2-week wash-out control period in between. Subjects were fed 30 g a day of either coarse wheat bran or fine wheat bran. Fasting blood samples were taken on day 14 of each 2-week period. On fine wheat bran total cholesterol (TC), as compared to control, was 1.57±1.96% higher in the males (ns), 3.30±2.22% lower in the post-menopausal females (ns) and 4.51±1.78% lower in the pre-menopausal females ($p<0.02$). Coarse wheat bran had no effect on TC. Neither wheat bran, when compared to control, had any effect on serum triglycerides or HDL.

	Total Cholesterol (mmol/L)		
	Males	Pre-Fem	Post-Fem
Control	4.69±0.23	4.95±0.18	5.70±0.35
Coarse	4.78±0.24	4.83±0.21	5.65±0.36
Fine	4.72±0.20	4.71±0.16	5.49±0.32

Fine-ground wheat bran may lower serum cholesterol in pre-menopausal females.

NU3

THIAMINE DEFICIENCY AND SUPPLEMENTATION IN INTENSIVE CARE UNIT (ICU) PATIENTS. D. R. Wong,* C. D. Mazer, K. Jeejeebhoy. Departments of Anaesthesia and Gastroenterology, St. Michael's Hospital, Faculty of Medicine, University of Toronto, Canada, M5B 1W8.

Thiamine (vitamin B_1) is an important metabolic coenzyme (as thiamine pyrophosphate, TPP), and its deficiency has been linked to poor clinical presentation in certain disease states, including congestive heart failure with diuretic therapy. This clinical prospective study examined 15 ICU patients to determine the thiamine status of this diverse group of critically ill patients, and the effect of 200 mg iv thiamine supplementation. Results of serum thiamine (7.72 ± 6.93 nmol/L) and packed RBC TPP (thiamine pyrophosphate, 78.49 ± 22.54 ng/mL packed RBC) suggest that these patients have low thiamine levels compared to previously published normals (22-38 nmol/L and 123 ng/mL packed RBC, respectively), but that thiamine levels increase 24 hours following thiamine supplementation. In addition, thiamine excretion appeared to be increased as evidenced by urinary thiamine metabolite levels. No conclusive correlation between improved thiamine and clinical statuses was found in this small population sample.

OBSTETRICS AND GYNECOLOGY

OG1

POSTNATAL OUTCOMES FOLLOWING IN UTERO RELEASE OF OBSTRUCTIVE UROPATHY. CK. Cheung*, DF. Geary, S. Grisaru, G. Ryan. Department of Pediatric Nephrology, The Hospital for Sick Children, and Department of High-Risk Obstetrics, Mount Sinai Hospital, Faculty of Medicine, University of Toronto, Canada M5G 1X8.

The growing detection of bilateral fetal obstructive uropathies by ultrasound has permitted the identification of pregnancies which would benefit from in utero urinary decompression. However, there is little information on the severity of postnatal renal dysfunction and none on the quality of life resulting from such interventions. This retrospective report examines the indications for antenatal intervention and outlines the postnatal course of all children who underwent in utero vesicoamniotic shunting for relief of fetal obstructive uropathy at the University of Toronto. Factors studied included: postnatal survival and renal function, physical growth and developmental status, method of feeding and voiding, number of hospital days and procedures, and other medical problems. Shunting was performed in six fetuses between 1994-1995, at gestational ages ranging from 20-28 weeks. Four children had posterior urethral valves (PUV), 1 Prune Belly Syndrome and 1 urethral agenesis. Fetal urine chemistry was an inconsistent predictor of postnatal renal function. One baby died at day one due to hypoplastic lungs and urethral agenesis. Another with PUV died at age 2.1 years due to sepsis following renal transplantation. Four children are alive, ranging from 0.7-2.4 years with creatinine levels 40-309 umol/L. Of the 5 who survived at least 6 months, 2 with persisting severe renal dysfunction were growth-retarded with delayed gross motor development. These 2 children required gastrostomy tube feeding. Total duration in hospital ranged from 27-93 days, representing 5.7-12.1% of life lived. All voided via a pyelostomy or vesicostomy. Additional medical problems included: hydrocephalus, gastro-esophageal reflux, metatarsus adductus, torticollis and features of Potter's syndrome. This study illustrates the variable quality of life and severity of renal dysfunction following antenatal in utero urinary decompression. This information is mandatory for those counseling parents-to-be and for accurate evaluation of antenatal intervention.

OG2

HOW HAS CLINICAL PRACTICE CHANGED (1980 to 1994) FOR POSTTERM PREGNANCY?. A.K. Sue-A-Quan*, M.E. Hannah, M.M. Cohen, J. Hellmann, R. Liston. Dept. of Obstetrics and Gyenaecology, Faculty of Medicine, University of Toronto, Canada.

Evidence from meta-analyses of randomized controlled trials (published since 1992) suggests that a policy of induction of labor at ≥41 weeks gestation will decrease the probability of stillbirth and will not increase (and may decrease) the likelihood of cesarean section. We wished to determine if clinical practice in Canada (1980-1994) has changed, consistent with the evidence i.e. an increase in the proportion of births at 41 wks and a decrease at ≥42 wks and to determine if there has been an associated decrease in stillbirth rate.

STUDY DESIGN: Information on live births and stillbirths by gestational age at delivery was obtained from Statistics Canada for the years 1980-1994. The proportion of births at 41 and ≥42 wks was determined for each year. The proportion of women having a stillbirth at ≥41 wks was also examined. The changes in rates over time were analyzed using linear regression. A $p<0.05$ was considered to indicate statistical significance.

RESULTS: The proportion of births occurring at ≥41 wks in Canada has not changed over the past 14 years. However, the percentage of births occurring at 41 wks has significantly increased (1980: 11.9%, 1994: 16.2%, $p<0.0001$). The percentage of births at ≥42 wks has significantly decreased (1980: 7.14%, 1994: 3.6%, $p< 0.0001$). The overall stillbirth rate for births ≥41 wks has decreased significantly (1980: 2.8/1000, 1987: 2.0/1000, 1994: 1.2/1000, $p<0.0001$).

CONCLUSIONS: Clinical practice has likely changed consistent with the research evidence, and neonatal outcome has improved. These data suggest that more women are having labor induced electively at 41 wks ($41^{0}/_{7}$-$^{6}/_{7}$). Other explanations for the observed changes may be increased use of fetal monitoring followed by induction of labor or changes in methods of dating the pregnancy. The decrease in stillbirth rate is likely a result of fewer women progressing to 42 or more weeks of pregnancy. This study suggests that obstetrical practice in Canada has been responsive to evidence-based research

OG3

META-ANALYSIS OF RCTS: INDUCTION OF LABOUR VERSUS EXPECTANT MANAGEMENT FOR PRELABOUR RUPTURE OF MEMBRANES (PROM)

B. Tan*, M. Hannah, Women's College Hospital, Faculty of Medicine, University of Toronto

OBJECTIVE: To determine the effects of induction of labour versus expectant management for PROM on maternal and perinatal morbidity, and to compare different induction methods.

METHODS: The world literature was reviewed for randomized controlled trials that compared induction of labour with prostaglandins (PG), induction of labour with oxytocin (OX) and expectant management (EXP) for PROM. Computer and manual searches were conducted in accordance to the strategy developed by the Cochrane Collaboration Pregnancy and Childbirth Group. Studies were selected if they included women with spontaneous rupture of membranes, before labour, ≥ 34 weeks gestation. Trials were assessed for quality and data were abstracted. For each outcome variable, a typical odds ratio (TOR) and 95% confidence interval (CI) were calculated.

RESULTS: Forty-three studies were included for analysis. The results are reported below:

OUTCOME	PG vs EXP			OX vs EXP			PG vs OX		
	S	TOR	95% CI	S	TOR	95% CI	S	TOR	95% CI
Epidural Analgesia (E/A)	7	1.01	0.89-1.15	7	**1.20**	1.06-1.35	8	**0.85**	0.73-0.98
Caesarean Section (C/S)	15	0.95	0.79-1.14	18	1.16	0.99-1.36	16	0.88	0.71-1.09
Chorioamnionitis (C)	8	**0.77**	0.61-0.97	12	**0.63**	0.51-0.78	6	**1.49**	1.07-2.09
Endometritis (E)	9	0.77	0.56-1.05	11	**0.72**	0.52-0.99	8	1.13	0.76-1.67
Neonatal Infection (N/I)	12	0.90	0.63-1.30	14	**0.64**	0.44-0.93	7	1.58	0.98-2.54
Perinatal Mortality (P/M)	6	0.22	0.03-1.79	8	0.20	0.03-1.26	4	n/o	n/o

S = Number of Studies n/o = No Outcomes **bolded numbers** = statistically significant result

CONCLUSIONS: Induction of labour with PG decreases the risk of maternal infection (C) compared to EXP management. Induction of labour with OX increases the risk of maternal intervention (E/A) and decreases the risk of maternal infection (C,E) and adverse perinatal outcome (N/I) compared to EXP management. Induction of labour with PG decreases the risk of maternal intervention (E/A) and increases the risk of maternal infection (C) compared to induction of labour with OX. There is no evidence that either induction of labour with PG, induction of labour with OX, or EXP management increases the rate of C/S or P/M. Women with PROM should be informed of the benefits and risks associated with induction of labour with PG, induction of labour with OX and EXP management and be encouraged to choose the treatment option they would prefer.

ON1

FREQUENCY OF MICROSATELLITE INSTABILITY IN HUMAN GASTRIC CARCINOMAS IN CENTRAL-EAST ONTARIO. C.B. Betel*, N. Di Nicola, M. Redston, S. Gallinger. Samuel Lunenfeld Research Institute, Departments of Pathology and Surgery, Mount Sinai Hospital, Faculty of Medicine, University of Toronto, Canada M5G 1X5.

Hereditary non-polyposis colorectal cancer (HNPCC) comprises 4-6% of all colorectal cancer cases. It is caused by defects in the DNA mismatch repair (MMR) system, a system that normally replaces incorrect nucleotides during DNA replication. In HNPCC patients, germline MMR gene mutations lead to accumulations of somatic mutations in oncogene and tumour suppressor genes, resulting in an elevated cancer risk. The hallmark of somatic mutations caused by MMR gene defects is referred to as microsatellite instability, demonstrated as electrophoretic mobility shifts in PCR-amplified tumour DNA from HNPCC patients (also called replication error positive, RER+). Other than the high frequency of colorectal cancer in HNPCC, these patients have high rates of gastric cancer. Identification of HNPCC cases has important clinical implications in the prevention of cancer in genetically predisposed individuals and their families. The purpose of this study was to determine the frequency of RER+ gastric tumours within a population based retrospective cohort of young (less than 55 years old) gastric cancer cases in Central-East Ontario from 1988 to 1992. Tumour and normal DNA was extracted from paraffin-embedded samples, amplified by PCR at five to nine microsatellite repeat loci, and run on a polyacrilimide gel. The normal and tumour lanes were compared, and differences between the two were identified as being either RER+ or loss of heterozygosity (LOH). Although literature primarily from the Far East suggests that the frequency of RER+ gastric tumours lies between 15-39%, our study determined that only 3 (7.9%) out of 38 gastric tumours were RER+. This discrepancy highlights the referral bias intrinsic to population based cancer molecular genetic studies and also suggests differences in pathogenesis between North America and Asian gastric cancer

ON2

LETHALITY OF WELL-DIFFERENTIATED THYROID CANCER I.B. Rosen, D.L. Chen*, J.L.Freeman, P.G. Walfish. Departments of Surgery, Otolaryngology, and Medicine, Mount Sinai Hospital, Faculty of Medicine, University of Toronto, Canada M5G 1X5.

Well-differentiated thyroid cancer (WDC) consists of papillary and follicular carcinoma which is frequently discounted for lethality which undermines an aggressive attitude in the management of this disease. A retrospective review of patients with WDC was carried out with particular attention to lethal cases. Patient histories were reviewed for such factors as gender, age, delay in diagnosis, pathology, tumor, and treatment factors. Comparisons were made between 100 alive patients and our own mortality group. Of 600 WDC patients encountered over the last 30 years, 23 deaths occurred for a frequency of 4% consisting of 8 males and 15 females. Pathology consisted of follicular CA 2, Hurthle cell CA 2, "anaplastic" CA 2, papillary CA 17. Mortality factors included age >60, presenting systemic involvement 5, eventual systemic involvement 13, metastatic cervical nodes 14, recurrent disease 14, extrathyroidal invasion 16, delay in diagnosis 23, previous treatment 6, inadequate treatment 15, tall cell histology 3. Postop RAI was given in 11, external radiation 15. Course of patients with lethal WDC was frequently prolonged and unexpected in cancer behavior. WDC is an infrequent cause of lethality. Scrutiny of predictive factors cannot establish course for the individual. In view of this, optimal treatment plan consisting of early FNAB, non-reliance on biopsy only, total thyroidectomy, node sampling, and RAI appears indicated particularly because of low morbidity.

ON3

ESSIAC Use Among Cancer Patients in Ontario

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ESSIAC, a herbal tea made from sheep sorrel, burdock root, slippery elm bark and turkey rhubarb root, was developed by Rene Caisse a Bracebridge, nurse in 1924 and used as an 'alternative' cancer remedy by her for over 50 years. ESSIAC remains the most commonly used 'alternative' cancer remedy in Ontario. In this study 360 patients with breast, prostate or gastrointestinal cancers attending outpatient clinics at Princess Margaret Hospital were surveyed regarding their experiences with ESSIAC. Patients who had ever taken ESSIAC then underwent a detailed interview about their expectations and experiences with this therapy. Overall, 58 (16.1%) had taken ESSIAC, while an additional 72 (20%) had heard of it. Patients with gastrointestinal cancer were most likely (24%) to have taken ESSIAC. No gender differences were seen. ESSIAC was taken more commonly in patients undergoing active treatment for their cancer. Most patients taking ESSIAC had heard about the remedy from friends or relatives. Almost 2/3 (66%) had heard of ESSIAC as a cure or possible cure for their condition. Other claims included improvement of overall well being (19%), boosting the immune system (9%) or to cleanse toxins from the body (11%). ESSIAC was well tolerated - no patients reported any adverse effects other than a mildly unpleasant taste, and patients on average spent $50 per month on the tea. When asked what the patients hoped ESSIAC would do for them, 32% hoped it would cure their cancer, another 32% hoped it would help in some way, the remainder had minimal or no expectations of any benefit. Of patients taking ESSIAC, 30% felt it had helped them. Of these the benefit was psychological in 54%, physical in 29% and unspecified in the remainder. One third of patients had asked their physician for information about ESSIAC and one half had informed their doctor they were taking it. Almost one-third of patients taking it feel it has helped them either physically or psychologically. Patients do look to their physicians for information and assistance in deciding whether to take alternative remedies, therefore doctors need to be knowledgeable in this area. Studies using validated quality of life scales examining the benefits of alternative remedies like ESSIAC are warranted.

ON4

THE SIMPSON-GOLABI-BEHMEL SYNDROME GENE OCI-5: REGULATION OF CELL GROWTH/APOPTOSIS AND INDUCTION BY CELL SHAPE CHANGES AND TRANSCRIPTION ELONGATION.

M. Li*, R. Pullano, B. Choo, J. Filmus and R.N. Buick. Ontario Cancer Institute/Princess Margaret Hospital and Department of Medical Biophysics, Faculty of Medicine, University of Toronto, Toronto.

OCI-5/Glypican 3 is the defective gene in Simpson-Golabi-Behmel Syndrome, a condition characterized by systemic overgrowth, developmental anomalies and a predisposition for childhood tumours. OCI-5 is believed to be involved in growth control during morphogenesis and/or tumour suppression. In the intestinal epithelium, expression of OCI-5 exactly correlates with events in morphogenesis. To investigate the mechanism of its regulation in the developing intestine, OCI-5 expression was studied in primitive rat intestinal epithelial cell lines. A large induction of OCI-5 is observed at confluence. Cellular analysis of this phenomenon implicates a role for cell shape in the induction of OCI-5, where a more rounded morphology results in an increase in OCI-5 gene transcription. Nuclear run-on analysis probing different regions of the gene demonstrate that release of an elongation block contributes to the induction of OCI-5 with confluence and growth/survival analyses of cells expressing OCI-5 suggest a role in slowing cell growth and/or apoptosis. Cell shape changes represent a convenient and temporary signal for the regulation of critical genes during morphogenesis, and elongation control is a rapid mechanism for executing this regulation at a time when gene-specific transcription initiation factors may not yet be established. Such a complex regulation reflects the importance of OCI-5, which these data suggest may be tumour suppression through regulation of cell growth and apoptosis.

ON5

THE ROLE OF $p16^{Ink4a}$ IN THE PROLIFERATION AND DIFFERENTIATION OF MALIGNANT ASTROCYTOMA CELLS.

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$p16^{Ink4a}$ (p16) is a tumor suppressor gene that is frequently lost in malignant astrocytomas. We have previously shown that the p16 deficient malignant astrocytoma cell line U343 MG-a (U343) differentiates in response to retinoic acid (RA) treatment. Differentiation of this cell line with RA is associated with morphologic change characterized by formation of cell processes and reorganization of the cytoskeleton due to an altered pattern of expression of glial fibrillary acidic protein (GFAP). RA treatment also causes reduced proliferation associated with increased expression of cyclin-dependent kinase inhibitors (CDKIs) $p21^{Cip1}$ and $p27^{Kip1}$. In order to determine the effect of restoration of expression of the CDKI p16 on the proliferation and differentiation of U343 cells, we induced p16 expression using the tetracycline repressor system. Using this system, p16 protein expression was detected by western blot analysis within 12 hours of induction. Induction of p16 expression potently arrested cells in G1 phase of the cell cycle as determined by growth curve and flow cytometry analysis. In addition, p16 induction was associated with formation of large, flat cells uncharacteristic of the parental cells. These large, flat cells exhibited a dramatic reorganization of the cytoskeleton, as shown by an altered pattern of immunofluorescence staining for GFAP. Co-treatment of p16-expressing cells with RA caused marked alteration in cell morphology characterized by an arrangement of cell processes and alteration of GFAP expression, suggesting that p16-induced growth arrest facilitated terminal differentiation. In order to see if the induced p16 expression was associated with alteration in expression of downstream cell cycle regulatory proteins, we also performed western blot analyses for the Retinoblastoma /E2F family of proteins. A rapid decrease in expression of the Retinoblastoma/E2F family proteins pRB, p107, and E2F1 with a shift to hypophosphorylated forms was found. No change in expression of p130 or other E2F species was noted. We conclude that induction of p16 expression in U343 astrocytomas fails to induce differentiation but profoundly arrests cell proliferation mediated by a discrete pathway involving pRB, p107, and E2F1. Also, the flat cell morphology associated with p16 expression suggests that this cell phenotype may depend only on the state of cell cycle arrest.

PAEDIATRICS

PD1

AN EVALUATION OF LINEAR VENTRICULAR VOLUME ESTIMATES. B.B. O'Hayon, J. Drake. Division of Neurosurgery, The Hospital for Sick Children, Faculty of Medicine, University of Toronto, Canada M5G 1X8.

The diagnosis of hydrocephalus in children, whether congenital, acquired or a complication of shunt infection relies on an accurate means of ventricular volume estimation. Linear estimates have been categorized as being too simplistic an assessment of ventricular volume because of the nature of ventricular expansion in hydrocephalus. However, studies have demonstrated clinically relevant linear measurements when analyses include only ventricular widths most reflective of ventricular expansion in hydrocephalus. Since linear measurements offer a practical and easily applicable estimation of ventricular volume, they have the potential to increase diagnostic power in clinical situations. We compared various linear measurements with the gold standard estimation of ventricular volume and determined that the most valid linear estimation of ventricular volume is a ratio of the frontal and occipital horn widths to the maximum intracranial width, the *ventricular volume measurement* (VVM).

PSYCHIATRY

PS1

ACQUIRED ATTENTIONAL DEFICIT ASSOCIATED TO CNS PROPHYLACTIC TREATMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A PILOT STUDY. D. A. Bowlby*, A. Ickowicz, R. Tannock, B. Spiegler, M. Greenberg. Department of Psychiatry, The Hospital for Sick Children, Faculty of Medicine, University of Toronto, Canada M5G 1X8.

Hypothesis: Children treated for ALL with cranial radiation (CR) will differ from children treated with high-dose IV methotrexate (MTX) with respect to the extent of accompanying inattention, impulsivity and hyperactivity. *Objectives:* Determine number of children who received CNS prophylaxis for ALL and develop impairments in attention and concentration; how many meet diagnosis of ADHD, exhibit specific cognitive deficits associated with ADHD (inhibitory control and working memory) and whether children treated with CR differ from children treated with MTX with respect to the relative severity of inattention, impulsivity and hyperactivity. *Methods:* A sample of 10 children, aged 7 to 11 at study, diagnosed and treated with CNS prophylactic therapy for ALL currently in stable long-term remission were recruited from the Oncology registry at HSC. Evaluation included clinical diagnostic interviews conducted with the child's parents and teacher, as well as direct measures of overt behaviour, cognitive profile, anxiety and depression. *Results:* Two children treated with MTX met diagnostic criteria for ADHD while none did in the CR group. Children in the CR group were less active. The MTX group showed greater impairments in inhibitory control and working memory. There was an over-representation of anxiety symptoms in both groups. *Conclusions:* Preliminary data is suggestive of clinical differences between the MTX and CR groups, the MTX group showing findings associated with frontal cortex function.

PS2

CLINICAL RATING SCALES IN THE EMERGENCY ASSESSMENT OF SUICIDAL RISK. K. Cochrane*, J. Lofchy, I. Sakinofsky. Emergency Services, The Clarke Institute of Psychiatry, Faculty of Medicine, University of Toronto, Canada M5T 1R8.

The evaluation of suicidal patients is a critical aspect of emergency psychiatric care. Patients at high risk for suicide should not be discharged because they are managed most safely in the hospital setting. Experienced psychiatrists usually evaluate suicide risk through the course of a complete psychiatric history, and using their own criteria. However, the use of standardized clinical rating scales (e.g. The SAD PERSONS Scale) may be an effective adjunct to emergency assessment, especially for the less experienced (vis a vis psychiatry) health care providers (e.g. clinical clerks, family physicians). Although there are well over 20 recognized "suicide prediction" scales, reviews of their utility are relatively sparse. The purpose of this study was to determine whether clinical rating scales may be useful tools in the emergency assessment of suicidal risk. A comparison was made between identification of high risk patients by six clinical scales and experienced psychiatrists and staff at the Clarke Institute of Psychiatry. This information is the first step in determining whether these scales should be used more widely and systematically in the emergency assessment of suicidal risk. Subjects were obtained through the Clarke Institute of Psychiatry Emergency Services. The clinical rating scales were administered to consenting adult patients (18-64 years) representing consecutive emergency assessments between 11 am and 9 pm (week-days for 2 months, n=59). For this patient population, the clinical rating scales had high sensitivity (range=75-100%) and high negative predictive value (range=88-100%). However, their specificity and positive predictive value were lower (range=38-85% and 26-60%, respectively). Clinical rating scales cannot predict suicide (a rare event), and they may be too liberal in their assessment of suicidal risk, but they highlight important information for consideration.

PS3

Children's Perceptions Related to Stimulant Treatment.

B.Hsi, B.Sc L.Zwaigenbaum, M.D., W. Roberts, M.D., Sarah Oosterhuis M.S.W. Developmental Pediatrics, The Hospital for Sick Children, University of Toronto.

Objective: Children with Attention Deficit Hyperactivity Disorder (ADHD) were assessed regarding their attitudes and perceptions related to their disorder and stimulant medication treatment.

Method: Fourteen children aged 9-13 with ADHD treated with stimulants, were studied while at a residential summer program. Individual structured interviews were conducted. Parameters studied included perceptions towards ADHD and stimulant medication, the social stigma of children on medication, and their attributions regarding medication effect and their behavior. Similar questionnaires were administered to the parents. Results were coded and analyzed by paired T-tests and Pearson Correlations.

Results: General attitudes towards stimulant medication were negatively correlated with age ($r=-0.54$, $p=0.036$). This relationship persisted after adjusting for confounding factors, including daily dose and self-reported side effects. Multiple regression did not show any other independent predictors of attitudes towards taking medication. Children with the highest level of self-reported side effects attributed greater control over aspects of their daily functioning more to medication versus personal effort ($r=-0.63$, $p=0.039$) Parents' perceptions of their children's attitudes reflected their own opinions more strongly than those of their children ($t=2.21$, $p=0.047$). Parents also attributed greater importance in their children's behavioral control to medication effects than did their children. Self and parent reported side effects were similar except for: 1)talks less with others (social withdrawal) ($t=2.85$, $p=0.015$) and 2) adverse changes in emotional state($t=2.38$, $p=0.035$).

Conclusions: As children become older there is an increasing negativity towards their use of medication. Children were more likely than parents to attribute success to their own effort rather than to medication effect. However, children with higher levels of self-reported side effects were more likely to attribute their behavioral control to medication. In general, parents perceived their children to be more negative towards ADHD and their medication than children themselves reported. These differences in perceptions may reflect lack of insight of parents into their child's feelings and raises questions regarding the validity of relying on parent reports in treating children with ADHD.

RA1

MR VOLUMETRY OF FRONTAL LOBE REGIONS IN ALZHEIMER'S PATIENTS: AN EFFECT OF SEX?, I.A.Y. Hall*, S.E. Black and S. Kohler, Sunnybrook Health Sci. Centre, Toronto, ON, Canada, M4N 3M5

Recent studies suggest that language functions may be more impaired in women than men with Alzheimer's Disease (AD). Using functional MRI, one report demonstrated sex-dependent variation in the activation of the inferior frontal gyrus (IFG) during phonological processing. Given that women demonstrate a pre-morbid advantage over men on some verbal tasks, the relative decline in women with AD is curious. We performed MR volumetry of frontal regions including; the superior frontal gyrus (SFG), middle frontal gyrus (MFG), IFG and inferior pre-central gyrus (PCG). Subjects were 9 males and 9 females who met NINCDS-ADRDA criteria for probable AD and an equal number of control subjects (NC) matched for sex, age and education.

Analysis was performed using ANALYZE software on images obtained from a 1.5 Tesla GE magnet. The volume of each gyrus was calculated by stereology (point counting) using serial 1.3 mm thick coronal sections on a T1 weighted 3D sequence. Data for each gyrus (right, left and total) were analyzed in 2-way ANOVAs (sex by group) using a total brain volume, age and duration of illness as covariates.

No significant effects or interactions were noted for the SFG, MFG or IFG. The total PCG was smaller in women than men [$F(1,27)=5.34$, $p<.02$] and smaller in the AD than NC group [$F(1,27)= 6.45$, $p<.02$], but there was no interaction. The left PCG demonstrated the same effect of sex [$F(1, 27)= 5.10$, $p<.02$] and group [$F(1,27)= 6.50$, $p<.02$] with no interaction. The right PCG showed no main effects or interaction.

The PCG is known to mediate some degree of motor processing for the lips, tongue and facial musculature. Although the interaction did not reach significance, the general direction of the data may suggest that women have a PCG which is smaller and more efficient for processing verbal/language information than men. A relatively small insult to this area may lead to a disproportionate loss of function as is seen in AD women compared to AD men. We are expanding our sample size to test this hypothesis. This project was funded by the Ontario Mental Health Foundation.

RA2

DUAL-ENERGY X-RAY ABSORPTIOMETRY ASSESSMENT OF PERIPROSTHETIC BONE REMODELING AROUND DISTAL FEMUR TUMOUR PROSTHESES. F. Lan*, A. Davis, J. Wunder, E. Cohen, M. Ichise, W. Cole, L. White, and R.S. Bell. Division of Orthopedic Surgery, Department of Surgery, Mount Sinai Hospital, Faculty of Medicine, University of Toronto, Canada M5G 1X5

Introduction. The Kotz modular femur and tibia reconstruction system (KMFTR) is a cementless prosthesis used bone tumour limb salvage procedures. Primary diaphyseal fixation can be achieved with or without cross screws. Dual-energy X-ray absorptiometry (DEXA) was proposed as a method of evaluating bone resorption due to stress shielding around the rigid femoral intramedullary stem.

Subjects and methods. 21 patients were studied. Mean age: 40.9 (20 to 74), mean time from operation: 30.1 months (8.00 to 60.50). 10 subjects had cross screw fixation, 11 had no screws. Male:Female=11:10.

Subjects were DEXA scanned on both the KMFTR leg (KL) and the contralateral leg (CL). Bone mineral density (BMD, in g/cm^2) was calculated in five regions of interest (ROI) along the femoral stem. For each patient, the BMD in each ROI of KL was standardized to the corresponding ROI in CL. DEXA precision was determined by performing repeated scans on 17 patients.

Results. Mean coefficients of variation for repeated scans ranged from 1.4% to 7.8% in the various ROI's.

Mean BMD in KL was significantly less than CL in 4 out of the 5 ROI's (greatest difference in the most distal ROI).

Patients without cross screws were found to have less %BMD loss at every ROI than those with cross screws, especially in the most distal ROI (where mean %BMD loss was 39.6% and 18.7% for the screw and non-screw groups respectively, $p=0.056$).

Discussion. DEXA is a precise method of evaluating BMD around KMFTR prostheses. Periprosthetic bone remodelling occurs to a significant extent, especially in the most distal ROI's, where one would expect the most stress shielding.

Patients with cross screws lost more bone than patients without screws, especially distally. A potential confounding factor for the screw vs. non-screw comparison was the length of follow up. Patients with cross screws had their prosthesis in situ for a significantly longer period of time than those without screws. However, all patients have been followed for at least 8 months and to date we have not seen increasing loss of BMD beyond 1 year.

RA3

3-D Real Time Visualization of Cerebral Aneurysms Using Quicktime Virtual Reality™

Amit Mehta*, David J Mikulis. Department of Medical Imaging, The Toronto Hospital - Western Division. Toronto, Ontario, Canada.

Purpose: Magnetic Resonance Angiography has evolved as a useful method to visualize cerebral vascular pathology. Post-acquisition manipulation uses specialized software and computer workstations to produce enhanced visual representations of these structures. The clinical utility of these images lies in their ability to allow the radiologist and surgeon to view vascular malformations in 3 dimensions and plan pre-operative techniques. Currently, software limitations prevent continuous real-time visualization in more than one plane of the 360 degree sphere; this serves to limit the utility of this technique as a pre-operative management tool.

Materials and Methods: We have developed a technique using Quicktime Virtual Reality software to allow real-time 3-D multi-planar visualization of vascular malformations. Images are generated from MRA studies are manipulated on a Sun Workstation to produce a user controlled 3-D movie.

Results/Conclusions: This new method enhances MR Angiography's utility both as a pre and post operative tool. It demonstrates to the clinician a true three dimensional representation of cranial pathology. It will strive to become a new standard in clinical imaging.

RA4

HIGH RESOLUTION ABDOMINAL MRI: OVERCOMING BREATHING AND ASSESSING EXPANSION OF AORTA DURING CARDIAC CYCLE.

E. Shin*, M.L. Wood. Sunnybrook Health Science Centre, Department of Medical Imaging, Faculty of Medicine, University of Toronto, Canada.

The research concerns high-resolution magnetic resonance (MR) images of the abdomen. Breathing causes abdominal organs to move in complicated patterns, but translation along the cranio-caudal direction dominates. We hypothesize that the blurring and ghosts caused by breathing can be reduced by reordering the sequence in which the data for an MR image are acquired. The approach was to test the suitability of a particular reordering method that corrects specifically for translational motion. Data for three-dimensional (3-D) images of the abdomen of a volunteer subject were acquired during periods of suspended breathing. The data for several images were reordered according to the displacement of the kidney to construct one hypothetical image. There was a slight reduction of ghosts and blurring in the resulting image. As a preliminary step in assessing the mechanical properties of blood vessels, high-resolution MR images of the aorta were acquired in synchrony with the cardiac cycle in healthy subjects. The cross-sectional area of the aorta was measured.

The hypothetical image obtained by the reordering method indicates that there is potential for this method to be used for abdominal MR images in patients where breath-holding is not possible. The aortic images indicate that it is possible to observe and measure the change in size and shape of the aorta during the cardiac cycle. Thus, high resolution MRI can be used to assess the mechanical properties of the aorta.

RA5

CD-ROM ON ARTIFACTS IN ULTRASOUND IMAGING.

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We produced an interactive teaching file to explain the physical reasons and clinical significance of artifacts in diagnostic ultrasound imaging. Artifacts in diagnostic imaging are defined as misrepresentations of the subject being imaged. It is inherent in all diagnostic images and a thorough understanding of its physical origins and clinical implications can improve the diagnostic accuracy of the diagnostician. Artifacts are often considered to be undesirable consequences of the imaging procedure; however, in ultrasound it can often aid in the diagnosis.

Using a highly interactive and user-friendly interface, a multimedia computer-aided learning file was created, using Authorware. Each artifact is introduced by showing the appropriate images. The student is asked to identify the artifact; this is followed by an optional discussion of the physical origin and the clinical implication. The content is divided into 5 major sections, covering both gray-scale and colour Doppler imaging. The program runs on a multimedia personal computer.

RA6

PHASE UNWRAPPING IN ELLIPTICAL POLAR COORDINATES IN RECONSTRUCTION OF MOTION-CORRUPTED MAGNETIC RESONANCE IMAGES.

K.W. Tam*, M. Wood. Division of Imaging Research, Sunnybrook Health Science Centre, Faculty of Medicine, University of Toronto, Canada M4N 3M5

In magnetic resonance (MR) imaging, the measured values are frequency data, each point of which affects the entire image; hence, the complete set of values must be taken together to create the MR image. The patient must remain motionless for the duration of the scan, which can be impractical for scans lasting up to several minutes. Minor patient movement (on the order of a few degrees of rotation) can critically compromise image quality, especially in functional MR imaging (fMRI), which measures brain activity based on brightness differences between successive scans of 2% or less.

Ongoing research at our lab has delved into methods for reconstructing MR images of the head corrupted by head motion. We model the head as a rigid body that undergoes instantaneous translation and rotation at a finite number of points in time during scanning. Reconstruction involves: 1) dividing the data into contiguous regions during which the head was motionless, 2) determining and compensating for the amount of translation and rotation, and 3) filling in values within regions newly created by the compensation step, for which there are no measured data.

The original research presented here suggests a method for filling in values within gaps created by motion compensation. The 2D image is manipulated in the frequency domain, which has magnitude and phase components; the latter, critical to reconstructing edges in the MR image, is confined by the nature of the data to values between -180 and +180 degrees –effectively a modulo operation. The head is assumed to be roughly elliptical, and, after aspect ratio compensation, is mapped onto polar coordinates. This allows improved extension of the phase component beyond the -180 and +180 limits, yielding improved interpolation.

RE1

HEAT STRESS CONFERS PROTECTION AGAINST VENTILATOR-INDUCED LUNG INJURY. K.Rhee*, S.P. Ribeiro, L. Tremblay, A.S. Slutsky. Division of Respiratory Medicine, Faculty of Medicine, University of Toronto, Toronto.

Ventilator-induced lung injury is a significant cause of morbidity and mortality in the intensive care setting. Research aimed at minimizing this type of injury has traditionally focused on altering the mechanical factors (pressure and volume) associated with lung injury. Recently, the role of cellular and molecular mediators have become the focus of investigations in ventilator-induced lung injury. Based on previous studies in our laboratory on the effect of heating or cytoprotection in sepsis, we examined the hypothesis that heat stress may have a protective effect on lungs exposed to mechanical stretch.

Methods: 40 Sprague-Dawley male rats were either given sham treatment, C, or heat stress , H (rectal temperature of 41°C for 15 min). 18 hr later, the lungs were harvested, compliance measured and the lungs were ventilated *ex vivo* (V_T=40cc/kg, 2 hr) in a humidified chamber at 37 °C; thereafter, static compliance was measured and the lungs were lavaged.

Results: Control lungs, C, showed a 47% decrease in lung compliance (pre- vs. post-ventilation) and an increase in post-ventilation lung lavage levels of TNF-α (722±306 pg/ml), IL-1β (9023±22) and MIP-2 (363±104). *Ex vivo* ventilated lungs from rats exposed to heat stress, H, showed only a 20% decrease in lung compliance and a decreased level of cytokines in the lung lavage, post-ventilation: (TNF-α= 233±119pg/ml; IL-1β= 124±53; MIP-2 73±52; $p<0.037$).

Conclusion: We conclude that exposing animals to heat stress confers protection against mechanical ventilation-induced lung injury possibly by a mechanism involving attenuation of cytokines.

National Sanitarium Scholarship

SU1

SEVERE LOWER EXTREMITY TAUMA: EVALUATION OF AMPUTATION INDEXES AND PATIENT OUTCOMES A. Best, A. Dagum (MD), M. Mahomed (MD), J. Mahoney (MD), E. Schemitsch (MD). Dept. of Plastic and Orthopaedic Surgery, St. Michael's Hospital, Faculty of Medicine, University of Toronto, Canada M5B 1W8.

Severe Open Tibial Fractures (Gustilo IIIb, IIIc) when successfully salvaged are associated with severe morbidity. Many surgeons feel an immediate primary below knee amputation should be done at the time of injury to avoid the prolonged hospitalization and multiple surgeries associated with limb salvage. Several amputation indexes, based on arterial, nerve, soft tissue injury, fracture type and associated injuries have been developed to aid the trauma surgeon in making this decision. If the score is greater than a certain number then primary below knee amputation is recommended - if it is less, leg salvage is attempted. The purpose of this study was to evaluate the predictive effectiveness of primary amputation index scores of salvaged Gustilo IIIb, and IIIc open tibial fractures and the longterm patient outcome based on specific health status questionnaires. A retrospective chart review was carried out on 44 patients with open tibial fractures requiring muscle flap coverage or vascular repair, treated at SMH in the period between 1984 and 1995. The MESS, MESI, PSI, LSI amputation index scores were calculated for these patients. All the amputation index scores except for the MESI were found to be poor predictors of which patients would go on to require amputation.

40 of the 44 patients with a minimum of a one year follow-up were contacted and two validated questionnaires (WOMAC, SF-36) and a custom designed questionnaires were administered to gage pain, physical disability and quality of life. A high level of morbity was found in this group of limb salvage patients as measured by the combined physical score of the SF-36 and WOMAC. In conclusion, this study showed that amputation index scores are a poor predictor of which patients willl have a successful limb salvage or primary amputation. These scores should not be used in isolation by the primary surgeon to base his/her decision on amputation versus leg salvage. The longterm pain and disability of these patients is greater than previously thought but they still are more content to have their leg salvaged than amputated.

SU2

A RETROSPECTIVE REVIEW OF A NEW PEDICLE SCREW INSTRUMENTATION SYSTEM FOR POSTERIOR SPINAL FUSIONS. S. Bitting*, M. Ford. The Orthopaedic & Arthritic Hospital, Faculty of Medicine, U. of Toronto.

It is proposed that the Stryker Diapason pedicle screw instrumentation system is a safe, reliable system that significantly reduces the potential for neurologic injury and is useful in enhancing the probability of attaining a solid spinal fusion. This is a rod, pedicle screw, crosslink and hook system, composed of titanium alloy (Ti 6 Al 4V).

Pedicle screw systems have been in use for posterior spinal stabilization procedures since 1966. A large number of systems are currently available for use. The choice of a system is ultimately dependent on parameters such as ease of insertion and removal, safety, the ability to carry out postoperative imagining, as well as cost.

A retrospective review of the charts of 188 individuals who underwent spinal stabilization surgery at the Orthopaedic & Arthritic Hospital using the Stryker Diapason pedicle screw instrumentation system, was conducted. Intraoperative and postoperative surgical and hardware complications were examined. In order to assess hardware-specific problems a radiographic review was also performed which included assessment of screw micro-motion as indicated by presence of halos surrounding the screws. Previous studies have established the poor sensitivity involved in using imaging studies to establish the integrity of the fusion mass. Fusion mass integrity was only assessed in individuals who had undergone hardware removal and visual inspection of the fusion mass.

Intraoperative complications included dural tears (8) and nerve injury (1). Hardware complications included screws out (0), caps off (6), disengaged rods (5), and disengaged crosslinks (3). Out of 16 patients who had their hardware removed and their fusion mass inspected 14 had solid fusions and 2 had pseudarthrosis. Radiological review revealed 155 out of 1080 screws (14.4%) to have halos.

This review shows the Stryker Diapason system to compare favorably to other systems currently available both in terms of intraoperative and post operative complications. The low profile nature of the system with its minimal "fiddle" factor, ease of removal and ease of insertion are major advantages over other more complex systems.

SU3

OROMANDIBULAR RECONSTRUCTION: A CHALLENGE TO HEAD AND NECK SURGEONS. Mindy A. Black MSc, Jeremy Freeman M.D. Department of Otolaryngology, Mt. Sinai Hospital, Toronto, Ontario.

This study was undertaken to evaluate the applicability of the current techniques for oromandibular reconstruction.

The mandible is an integral part of the aerodigestive tract providing both function and cosmesis to the lower face. Specific indications for reconstruction can include neoplasm, osteoradionecrosis, trauma, and congenital causes. The challenge lies in recreating a "neomandible" that most closely approximates the qualities of the original. At present, the two most commonly used techniques for reconstruction include alloplastic metal plates often combined with a local flap, and autogenous vascularized osteocutaneous grafts. Ongoing refinement of these techniques has shifted concerns from primarily graft survival to now include a patient's post-operative ability to produce speech, deglutition, mastication, dental rehabilitation and cosmesis.

There are many options for oromandibluar reconstruction but no one method offers uniform applicability and success. Vascularized free tissue transfer provides the best chance for graft survival and patient rehabilitation. The use of metal reconstruction plates combined with a soft tissue flap remains an acceptable option in certain situations.

An algorithm is proposed to guide surgical decision making towards the method of oromandibular reconstruction with the optimum outcome for the patient. This algorithm takes into account patient factors such as age and general medical status; and disease factors such as prognosis and location of the defect. Finally, illustrative clinical cases drawn from the Mt. Sinai Head and Neck Surgery database are presented.

SU4

INTERCOSTAL NERVE DAMAGE AFTER AORTOCORONARY BYPASS SURGERY UTILIZING INTERNAL MAMMARY ARTERY GRAFT (IMA SYNDROME): PREVALENCE AND MORBIDITY. C. Boulias* and A Mailis, Pain Investigation Unit, The Toronto Hospital, Faculty of Medicine, University of Toronto, Canada M5T 2S8

Aim of Investigation: To assess the prevalence, evolution and time corse of chest wall pain associated with intercostal nerve damage (IND) after aortocoronary bypass surgery (ACB) with the use of Internal Mammary Artery graft (known as IMA syndrome)

Methods: Two groups of patients attending the cardiac rehabilitation program after ACB, other heart surgery or post myocardial event were recruited. Data were obtained via a) patient-completed survey and b) chest wall examination and analyzed for the presence of spontaneous pain, deep pain (on manual palpation), cutaneous abnormalities to cold, touch and pin prick perception, as well as the intensity and time course of nerve damage.

Results: The response rate to the survey was 61.5% (Group A = 40/65) and 85% of the responders had ACB-IMA surgery. Of the respondents 22 complained of chest wall pain in the past, 9/22 at present (41%) (all with ACB-LIMA) and 11/11 examined displayed evidence of IND. Of the 18 respondents with no pain complaints, 7/9 examined displayed evidence of IND (seen only in ACB-LIMA patients). With regards to all respondents in Group A, the prevalence of IND on physical examination was 86% and the prevalence of current spontaneous pain in those with IND 50%. A second group randomly selected (Group B = 45) for chest wall examination consisted of 35 patients with ACB-IMA and 10 with other procedures/event. 31/35 ACB-IMA patients displayed evidence of IND (88.6%). Of these patients 12/31 complained of deep (evoked) pain associated with spontaneous pain in 5/12 as well. Only 1/10 non ACB-IMA patients presented with deep pain on palpation in the absence of IND. In total, 71% of all examined patients with IND in Groups A and B displayed hypoesthesia to all sensory modalities, 13% hyperesthesia to all modalities and 16% co-existence of positive and negative sensory abnormalities. Cold hypoesthesia was the most prominent & persistent indicator of IND up to 2.5 yrs of follow-up post surgery.

Conclusions: The current technique of harvesting of the IMA for ACB is associated with significant morbidity due to intercostal nerve damage. The prevalence of IND is as high as 88.6% up to 2.5 years post surgery, while 50% of these patients complain of persistent chest wall pain or discomfort. Considering that 15,000 such procedures are performed yearly in Canada the lack of awareness of this neuropathic pain syndrome leads to unecessary and costly interventions targeting potential cardiac factors.

SU5

ACUTE INTESTINAL AND PULMONARY INJURY IN A MODEL OF RUPTURED ABDOMINAL AORTIC ANEURYSM. A. J. Boyd*, Ph.D. & T. F. Lindsay, MD, FRCS(C) Division of Vascular Surgery, Department of Surgery, Toronto Hospital (General Division), Faculty of Medicine, University of Toronto, Canada M5C 2C4.

Rupture of an abdominal aortic aneurysm (RAAA) is a lethal event in 90% of patients; with a significant proportion dying of multiple organ failure following successful repair. The purpose of this study was to determine whether the combined insults of hemorrhagic hypotension and aortic clamping, simulating RAAA repair, have a synergistic effect on the generation of local (intestinal) and remote (pulmonary) organ injury. Sprague-Dawley rats were hemorrhaged to a mean arterial pressure of 50 mm Hg for 1 hour, followed by 1 hour of supramesenteric aortic clamping (Shock + Clamp). Control animals were divided into Sham, Shock Only, and Clamp Only groups. Intestinal permeability was determined by measuring I^{125}-labelled albumin loss into an isolated, perfused segment of small intestine. Pulmonary permeability to albumin-I^{125} was determined by bronchioalveolar lavage. Intestinal and pulmonary myeloperoxidase (MPO) activity, an index of neutrophil infiltration and acute injury, were measured. Shock paired with supramesenteric aortic clamping resulted in a 5-fold increase in intestinal permeability compared with either shock or clamp alone. Furthermore, only the Shock + Clamp group showed an increase in pulmonary permeability, and this 3-fold increase was significantly correlated with the degree of intestinal injury. These results demonstrate the synergistic effect of shock paired with supramesenteric aortic clamping, which may explain the high rate of mortality associated with RAAA, and suggest that remote organ injury may depend on the degree of local organ injury.

SU6

PREDICTIVE FACTORS IN DETERMINING THE SURVIVORSHIP OF VALGUS HIGH TIBIAL OSTEOTOMY. B. Cho*, N. Wong*, Z. Agnidis, C. Hutchison. Division of Orthopaedic Surgery, Mount Sinai Hospital, Faculty of Medicine, University of Toronto.

High tibial osteotomy (HTO) is an orthopaedic operation used to realign the knee and alleviate the pain of unicompartmental osteoarthritis (OA) caused by a varus deformity. HTO is usually performed on younger patients with unicompartmental OA.

Purpose: This study was done to determine the length of time a HTO can be expected to survive before a TKA is required and to determine patient characteristics and radiographic measures which have the greatest predictive value in survival of HTO.

Methods: A retrospective chart review was carried out on patients who had undergone HTO, performed by one surgeon. A Kaplan-Meier survival analysis with a minimum two year follow-up was conducted.

Results: Out of 323 patients who had HTO, 31 were lost to follow-up. Sixty-two of the remaining 292 patients had undergone a TKA. The Kaplan-Meier survival analysis for HTO included 124 of the patients. At five years after HTO, 98% of patients had not gone on to TKA. At ten years, 88% had not gone on to TKA.

Conclusions: In this study , the need for a TKA was postponed for 10 years in 88% of patients following HTO. This supports HTO as an effective surgical procedure for delaying the need for TKA.

SU7

EXTRAUTERINE TWIN-TWIN TRANSFUSION AFFECTS RENAL FUNCTION AND PERIOPERATIVE MANAGEMENT OF CONJOINED TWINS. D.J. Klein*, R.F. Filler, D.F. Geary. **Departments of Pediatrics and Surgery, Hospital for Sick Children, Faculty of Medicine, University of Toronto.**

The aim of this investigation was to describe the occurrence of unbalanced circulatory shunting in 3 consecutively treated pairs of conjoined twins and, the effects of this phenomenon on renal function, timing of separation, and perioperative fluid management. Therefore, we reviewed 3 sets of conjoined twins (set 1 - craniopagus, sets 2 and 3 - omphalopagus) separated between 1994 and 1996 that had marked inequality of urine output before separation which significantly affected their management. Renal function was assessed by imaging studies and fluid balance was examined in detail. One twin (1A), aged 2.5 years, underwent renal transplant from his twin prior to separation because of persistent oligo-anuria and markedly shrunken kidneys. Emergency separation was necessary in set 2 at 7 days, after 2A became anuric. Set 3 was separated at 2 days of age because of a large omphalocele.

The following table shows urine output before and after separation in the 3 sets:

URINE OUTPUT (ml/kg/hr)

TIME	SET		SET		SET	
	1A	1B	2A	2B	3A	3B
1 day pre-op	0.3	5.6	1.9	16.5	1.1	4.8
1 day post-op	5.1	4.4	5.1	1.1	3.2	0.8

Each pair demonstrated a pre-operative polyuric state in the overperfused twin with an oliguric state in the underperfused twin. This reversed post separation, until urine output equalized after 1 to 3 days. Serum creatinine was similar in each pair before separation and was not a useful marker of individual twin renal function.

In conjoined twins renal function assessment is necessary and should include serial measurements of urine volume and urine excretion from each twin. Extrauterine twin-twin transfusion syndrome may lead to early renal failure in the underperfused twin and cardiac failure in the overperfused twin and must be considered in the timing of separation surgery. This phenomenon complicates post-separation fluid management.

SU8

FACTORS AFFECTING OUTCOME IN HIP REVISION ALLOGRAFTS

S.T. Sears*, S. Burch*, Z. Agnidis, A.E. Gross. **Division of Orthopedic Surgery, Mount Sinai Hospital, Faculty of Medicine, University of Toronto, Canada.**

The advantages of revision total hip arthroplasty (THA) with allograft include a better implant interface for cement, the potential for bone and muscle reattachment, the use of more conventional implant designs, and the restoration of bone stock. This retrospective study reviewed the surgical variables and patient characteristics of 494 patients who had undergone allograft hip revision. Potential risk factors for post-operative complications were evaluated.

All surgeries were performed by a single surgeon form 1983 to July 1996. Complications were defined as: infections, dislocations, nerve injuries. loosening of acetabular and/or femoral components, non-unions and fractures. The variables assessed were: age, gender, type of revision, type of graft, use of cement, use of roof reinforcement rings, and the number of total hip replacements. Multivariate logistic regression was used to evaluate predictors of complications with odds ratios reported for significant variables. A Kaplan-Meier survival analysis was also conducted.

Of the 494 allograft hip revisions, sixty three percent were acetabular and femoral revisions, 13% were femoral only, and 22% were acetabular only. There were 321 females and 173 males, with a mean age of 63 years. Complications occurred in 128 (26%) of the 494 surgeries. At five years after hip revision, 78% of surgeries had no complications. There were no apparent relationships between the incidence of complications and age. or gender. No significant correlations were shown between type of allograft. the use of cement, or the use of a roof reinforcement ring. The number of hip replacements was the most significant risk factor. From the second revision THA to the third revision there was two times the risk of a complication occurring, from the third revision to the fourth revision the risk of a complication increased 2.5 times, and from the fourth revision to five or more revisions, the risk of complication increased threefold. The type of revision was not a risk factor, however, among femoral revisions only, the risk of a complication decreased by one half.

The data suggests that the number of prior revisions may be an important factor associated with the risk of complication following allograft hip revisions. In addition, the incidence of complications was higher if the acetabular component had been revised.

SU9

EXTRACRANIAL HEAD AND NECK SCHWANNOMAS REPORTED CASES OVER THE LAST 25 YEARS

P.E. Spiess* MSc (9T9), M.J. Black, MD, G. Shennouda, MD. Division of Head and Neck Surgery, Department of Otolaryngology, Jewish General Hospital, McGill University, Canada.

Extracranial head and neck schwannomas are usually benign tumors originating from schwann cells. The number of reported cases in the head and neck have been limited and the aim of the present study was to examine the incidence of such tumors in three McGill teaching hospitals over the last 25 years.

The medical records of 39 patients who developed extracranial head and neck schwannomas were reviewed.

Of the 39 patients with schwannomas, 33 (85%) were benign and 6 (15%) were malignant. Most of the patients were females 24 (62%) and the mean age of patients was 43 years old. Most patients presented with pain due to the mass 35 (90%) and diagnosis was primarily based on clinical suspicion and imaging studies (CT and MRI). The most common sites of tumor were the sympathetic chain 12 (30%), cervical plexus 6 (15%), and vagus nerve 5 (13%). The 5-year survival rate for patients with benign schwannomas was 88% versus 16% for malignant tumors.

The present study showed that the surgical treatment of benign tumors was a very successful procedure with patients, 91% having no evidence of disease. However, malignant schwannomas have a poor prognosis regardless of the treatment modality.

SU10

OPEN vs CLOSED ACROMIOPLASTY FOR THE IMPINGEMENT SYNDROME: A CONTROLLED CLINICAL TRIAL. Khalid Syed * BSc, Richard Holtby MD, FRCSC and Peter Welsh MD, FRCSC, Orthopedic and Arthritic Hospital.

In 1972, Neer first described the impingement syndrome in which the tendon of the rotator cuff rubs on the acromion and as a result the tendon tears. Usually, it is the tendon of the supraspinatus that impinges on the acromion and is partially or completely tom. Neer also proposed acromioplasty as a method to prevent further tearing of the rotator cuff. In this procedure, the anterior part of the acromion is removed so that the impingement is relieved. In 1985, Ehlman described arthroscopic subacromial decompression (ASD) which is an arthroscopic procedure that accomplishes the same goal. Very little work has been done to compare the results of the two procedures with each other in a controlled clinical trial.

The purpose of this study is to compare open acromioplasty to ASD and to determine which of the two is better in terms of pain relief, functional recovery and patient satisfaction. The study is designed to be a controlled clinical trial in which 60 patients will be randomized for the two procedure. All surgeries of one type will be performed by the same surgeon to reduce experimenter bias. The patients will be followed up for two years and their recovery will be assessed at defined intervals. The comparison will be made in terms of both subjective and objective evaluations of the patient's condition by utilizing well recognized tools of shoulder assessment. These include the Constant scale of shoulder function, the UCLA shoulder scale and SF36 General Health Questionnaire. Other quality of life measures will also be used.

In general, a shorter recovery time and fewer complications are associated with arthroscopy. Arthroscopic procedures are also financially more feasible because they involve a shorter hospital stay and faster retum to work. Hence, proof of superiority of ASD over open acromioplasty may lead to more wide spread use of arthroscopic treatment for the impingement syndrome and can lead to lower costs for a better quality of care.

SU11

THE RELATIVE IMPORTANCE OF INTRAMEDULLARY, INTRACORTICAL, AND EXTRAOSSEOUS SOFT TISSUE BLOOD FLOW TO THE REPAIR OF DEVASCULARIZED CANINE TIBIAL CORTEX. J.A. Weinberg*, E.H. Schemitsch, M.D. McKee, R.R. Richards. Musculoskeletal Research Laboratory, St. Michael's Hospital, Faculty of Medicine, University of Toronto, Canada.

Previous studies have not quantified the relative contributions of intracortical and extracortical perfusion to cortical porosity and new bone formation. The current study was performed to determine the relative importance of intramedullary, intracortical, and extraosseous soft-tissue blood flow and type of tissue to the repair of devascularized canine tibial cortex. A 2.5-cm segment of tibia between two standardized osteotomies was devascularized. The segment was replaced anatomically and stabilized with a plate. The animals were divided randomly into two groups: skin coverage (n=8) and muscle coverage (n=8). Thirty-one days postoperatively Ce^{141} microspheres were injected, prior to sacrifice, to measure blood flow. Extraosseous soft-tissue perfusion was the same in the skin coverage and muscle flap coverage groups. There was no relationship between intramedullary or extraosseous soft tissue flow and depth of new bone formation and cortical porosity. Intracortical blood flow was directly related to depth of new bone formation ($p=0.0006$) and cortical porosity (outer cortex $p=0.001$; inner cortex $p=0.0001$). These findings indicate that the cortical repair process is linked to the restoration of perfusion and that muscle coverage, rather than the quantity of blood flow determines the extent of cortical repair.

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